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Original Communications

STUDIES WITH ARTERIOVENOUS FISTULAS

I. RESPONSE OF THE NORMALLY INNERVATED AND DENERVATED HEART TO OCCLUSION OF THE FISTULA

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THOUGH the medical profession was slow in becoming aware of the remote effects of arteriovenous fistulas upon the circulatory apparatus in general and of the possible harmful effects upon the heart in particular, once interest was aroused the circulatory dynamics in this condition were studied intensively both in experimental animals and in man. In spite of the important contributions which have been made, however, certain important facets of the problem remain obscure. In a study of patients with arteriovenous fistulas carried out during the last war Elkin and Warren[1] were able to make certain physiologic observations, including ballistocardiographic estimations of cardiac output. It was a striking fact that not only was the response of pulse rate and blood pressure almost instantaneous but the reduction in cardiac output similarly began immediately upon compression of the fistula. Because of the startling rapidity with which reduction in stroke volume occurred and the lack of alteration in right atrial pressure, Elkin and Warren reached the conclusion that "it appears to be a nervous reflex related to the sudden change in resistance against which the heart must pump."

The present communication deals with efforts to determine whether sympathetic denervation or both sympathetic and vagal denervation of the heart alters the response to digital occlusion of an arteriovenous fistula. It was hoped that this study would throw some additional light upon the mechanism of this response. It was also realized that any information which might clarify the circulatory dynamics associated with arteriovenous fistulas might promote a better understanding of the function of the heart and circulatory system in general and the influence of various stresses and strains.

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MATERIALS AND METHODS

Healthy adult mongrel dogs were used. They were maintained on a diet of commerical canned dog food. Operations were performed under intravenously administered pentobarbital anesthesia, a dosage of 25 mg. per kilogram of body weight being given. In those operations in which an open thoracotomy was necessary, an intratracheal tube was used and rhythmic inflation of the lungs with air was carried out by means of an alternating pressure respirator. All operations were done with rigidly aseptic technique.

In establishing the arteriovenous fistulas the femoral artery and vein were exposed and dissected free for a distance of several centimeters distal to the point of junction with the profunda femoral vessels. They were occluded proximally and distally with rubber-shod serrefine clamps. Longitudinal incisions were made in the opposing walls of the superficial femoral artery and vein and an anastomosis of these vessels was accomplished with everting mattress sutures of 00000 silk. The fistulas varied in length from 1.5 to 5.5 cm.; most of them were from 2 to 2.5 cm. long.

In 12 animals the sympathetic denervation was performed through upper dorsal thoracotomies, both sides being done, one after the other, at the same operation. The resected sympathetic chain included the fifth or sixth dorsal sympathetic ganglion at its lower end and the caudal cervical ganglion at its upper end (Fig. 1). In most instances the vagosympathetic trunks were exposed in the midcervical region at the time of the final study, loops of silk were placed about them to permit their subsequent future identification, and, at the appropriate time, they were completely divided. In one dog the vagosympathetic trunk was anomalous, being made up of several smaller trunks. In all instances care was taken to divide the trunks completely and such division was always followed by the characteristic slowing and deepening of respirations. In a few dogs only one vago-sympathetic trunk was sectioned and the other was blocked by direct infiltration with procaine solution; these animals were subjected to surgical division of both vagosympathetic trunks at a subsequent date. In 5 dogs bilateral division of the vagosympathetic trunks and resection of the sympathetic chains were carried out at one operation. The vagosympathetic trunks were divided above and below the point of connection with the caudal cervical ganglion. This ganglion, the stellate ganglion, and the upper five or six dorsal ganglia were then removed extrapleurally, more or less by blunt dissection, the rami to the dorsal ganglia being broken across with the dissecting finger.

At the completion of the experiments all of the animals were sacrificed and examined. The division of the vagosympathetic trunks and the extent of removal of the sympathetic chains were verified. The arteriovenous fistulas were examined and the size of the fistula was recorded.

All of the studies of cardiac output and of alterations in pressure and cardiac output upon digital compression of the fistula were made under pentobarbital anesthesia. The completeness of the digital occlusion was checked continuously by auscultation; in all instances the bruit was absent during such periods. The blood pressure recordings were direct measurements with a Hamilton manometer or an electromanometer. Oxygen consumption was determined by spirometric study over an eight-minute period. An intratracheal tube with an inflatable cuff was used and care was exercised to make sure there was no leak about the tube. Peripheral arterial blood and samples from the right ventricle or pulmonary conus were taken during the mid-portion of the study of oxygen consumption. The cardiac catheter was passed from the external jugular vein into the right ventricle or the pulmonary conus at the beginning of the study and the position of its tip was verified by fluoroscopic examination. Clotting was prevented by using syringes rinsed with heparin solution. The specimens were sealed in each syringe with mercury and a mercury-filled cap, and they were kept on ice until analyzed. The analyses of oxygen content and capacity were carried out promptly according to the technique of Roughton and Scholander.[2] Duplicate analyses were made on each specimen and additional analyses were performed in the occasional instance when they did not check within 0.2 volume per cent.

In 3 of the animals, splenectomy was performed at the beginning of the study and a number of estimations of blood volume, using the Evans blue dye T 1824, were made from time to time.

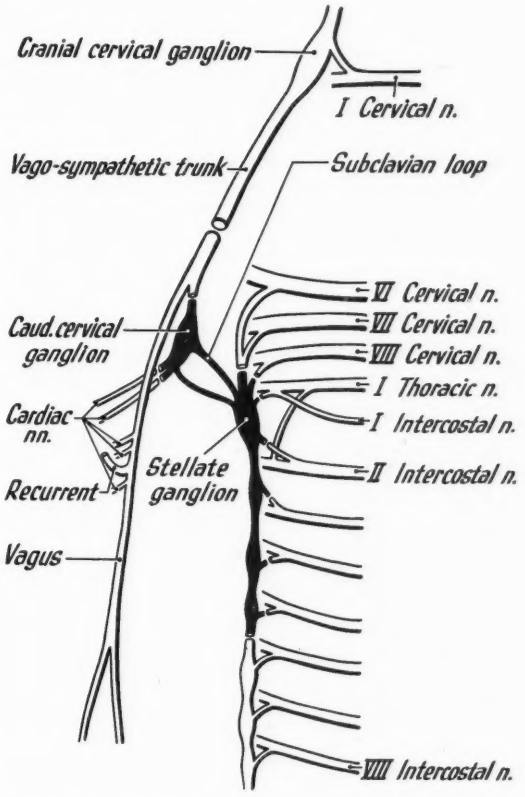

Fig. 1.—Diagrammatic representation of the upper portion of the vagosympathetic trunks. The point at which the vagosympathetic trunk is interrupted is shown, as well as that portion of the sympathetic chain which is resected.

RESULTS

In all animals used, the patency of the surgically produced fistulas was demonstrated by the presence of a typical continuous thrill and bruit. There was prompt recovery from the operation for sympathetic denervation. In those few animals in which determinations were made after sectioning one vagosympathetic trunk and anesthetizing the other, the animals also recovered rapidly. The animals were sacrified and examined after section of both vagosympathetic trunks and the studies which followed.

By and large, the determinations of cardiac output seemed satisfactory. Of approximately 150 studies of cardiac output, only 11 were excluded, 4 of which were performed upon normal dogs, 2 upon animals after the fistula had been created, 2 after sympathectomy had been performed, and 3 after sympathetic and vagal denervation. In the case of these excluded determinations it was obvious that some gross error had occurred, either because of leakage of oxygen or because of discrepancies in the blood oxygen analyses resulting in abnormally high or low arteriovenous differences.

TABLE I. RESPONSE OF CARDIAC OUTPUT AND BLOOD PRESSURE TO DIGITAL OCCLUSION OF ARTERIOVENOUS FISTULA IN DOGS WITH NORMAL CARDIAC INNERVATION, SYMPATHETIC DENERVATION, AND TOTAL EXTRINSIC DENERVATION OF THE HEART

NUMBER OF ANIMAL	STUDY OF CARDIAC OUTPUT BEFORE CREATION OF A-V FISTULA	LENGTH OF FISTULA IN CM.	INTERVAL IN MONTHS BETWEEN CREATION OF FISTULA AND STUDY OF CARDIAC OUTPUT	INTERVAL IN MONTHS BETWEEN CREATION OF FISTULA AND SYMPATHECTOMY	INTERVAL IN MONTHS BETWEEN CREATION OF FISTULA AND POSTSYMPATHECTOMY STUDY OF CARDIAC OUTPUT	INTERVAL IN MONTHS BETWEEN CREATION OF FISTULA AND STUDY OF CARDIAC OUTPUT AFTER VAGOSYMPATHETIC DENERVATION	RESPONSE OF CARDIAC OUTPUT TO OCCLUSION OF FISTULA			BLOOD PRESSURE RESPONSE TO OCCLUSION OF FISTULA
							NORMAL CARDIAC INNERVATION	SYMPATHETIC DENERVATION	TOTAL CARDIAC DENERVATION	
1	Yes	2.0	3.0	7.0	8.0	8.5 / 9.0	good	good	good	good
2	Yes	1.8	2.5 / 3.5	6.0	6.5	7.0	good	good	good	good
3	Yes	1.2	2.5	3.0	4.0	5.0	poor	varied	good	good
4	Yes	1.1	0.7	1.0		1.5	good		poor	good
5	Yes			0	0.2			good		fair
6	Yes	3.0	0.2	0.7	1.5	1.7	poor	good	varied	fair
7	Yes	3.4	1.5 / 2.0	2.0	2.5	2.5	good	good	good	good
8	Yes	2.0*	0.3	1.0	1.5	1.5	poor	poor	varied	poor
9	Yes	2.5*	0.7 / 1.2	2.0		2.2	varied		good	poor
10	Yes	3.4	0.5	1.5	1.7	1.7		good	good	good
11	No			0	0.2	0.2		poor	good	poor
12	No	5.5		1.5	1.7			good		good
13	No	2.2	8.0	8.0	8.0	8.0	good		good	good
14	No	3.0	7.0	7.0	7.0	7.0	good		good	good
15	No	1.6	7.0	7.0	7.0	7.0	good		poor	good
16	No	2.0	7.0	7.0	7.0	7.0	poor		poor	good
17	No	2.5	8.0	8.0	8.0	8.0	good			good

*Proximal vessels found to be occluded at post-mortem examination.

In Table I are briefly summarized the results of the study. In 10 animals the cardiac output was determined before creation of a fistula. The length of the fistula as measured at post-mortem examination ranged from 1.1 to 5.5 cm.; unfortunately the records of the length of the fistula in 2 dogs were lost. Listed also are the time intervals between the creation of the fistula and the subsequent procedures of measurement of cardiac output, sympathetic denervation, determinations of cardiac output after sympathectomy, and the final determinations after interruption of the vagosympathetic trunks. It will be noted that approximately one-half of the studies were completed within 2½ months after production of the fistula, while the other one-half were delayed 7 to 8 months. The response of the cardiac output to occlusion of the fistula was listed as good in those cases in which a significant decrease occurred. The response was listed as poor when either a slight decrease or a frank increase in cardiac output occurred and as varied when the results of duplicate or triplicate determinations were conflicting. The instantaneous changes in blood pressure following occlusion of the fistula are also tabulated. It will be noted that in 2 animals exhibiting no rise in blood pressure upon digital compression and in which the

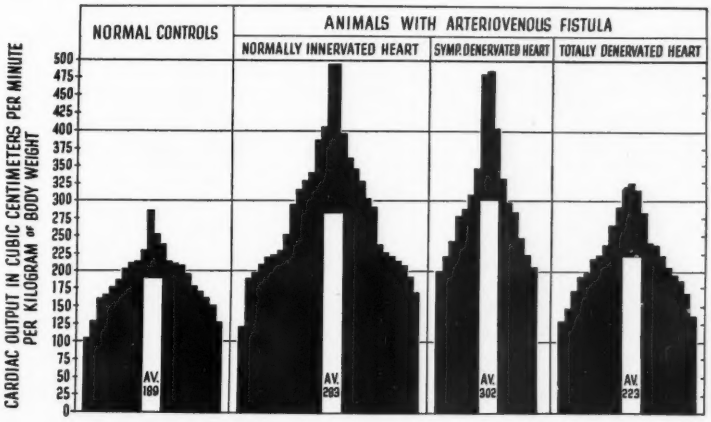

Fig. 2.—Values of cardiac output in normal dogs, in dogs with an arteriovenous fistula, and in such animals after sympathetic and total extrinsic cardiac denervation.

responses of cardiac output were more or less at variance with the majority of observations, the proximal artery and vein of the fistula were found to be occluded at the time of post-mortem examination though the fistulas were patent. The record of the condition of the fistula at the time the animal was sacrificed was unfortunately lost in a third instance in which there was no rise in blood pressure and in which the cardiac output rose slightly upon compression of the fistula on one occasion. In 3 dogs (No. 1, 2, and 5) several blood volume determinations were made before and after the fistula was created. In dog number 1 values beforehand were 124 and 131 c.c. per kilogram of body weight. Two months after the fistula was made the blood volume was 149 and 2 months later was 175. In the case of dog number 2 the preoperative blood volume was 101 c.c. per kilogram and 4 months after the fistula was made it was 125. The preoperative values were 105 and 110 in dog number 5 while 2 months after the fistula was produced the blood volume was 135 c.c. per kilogram.

In Fig. 2 are charted the values for cardiac output in normal dogs and in dogs following the production of an arteriovenous fistula and the subsequent operations for denervating the heat. There were 22 apparently valid determinations of cardiac output in 17 normal dogs in 10 of which studies were subsequently made after the production of a fistula

and after cardiac denervation. These 22 determinations, when expressed in cubic centimeters per minute per kilogram of body weight, ranged from 103 to 287 and averaged 189. In three fourths of them the values ranged from 150 to 230 and also averaged 189. In 13 dogs, in which fistulas had been established from 7 days to 3 months, 29 determinations of cardiac output gave values ranging between 168 and 495 c.c. per minute per kilogram of body weight, the average being 283. Only four of these estimations were below 210. Sixteen determinations of cardiac output were made from one week to 8 months after the production of the fistula in 9 animals in which sympathetic denervation had been carried out. These values ranged from 200 to 484 c.c. per minute per kilogram of body weight and averaged 302; only 2 were below 220. In the last group of 13 dogs with fistulas ranging in age from one week to 9 months and in which the vagal and sympathetic fibers to the heart had been interrupted, 22 determinations of cardiac output gave values varying from 147 to 320 and averaging 223; 5 were below 200.

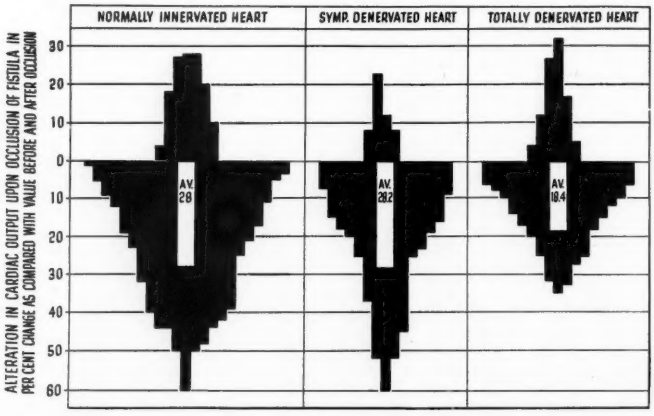

Fig. 3.—Alterations of cardiac output upon complete digital occlusion of the arteriovenous fistula in dogs with normally innervated, sympathetically denervated, and totally denervated hearts.

The alterations in cardiac output upon occlusion of the fistula are illustrated in Fig. 3; they are expressed in per cent change from the value determined immediately before or after occlusion. Thirty determinations of the response of cardiac output were made upon 13 dogs with normally innervated hearts. In 77 per cent a decrease occurred, the average reduction in cardiac output being 28 per cent. Following sympathetic denervation of the heart, occlusion of the fistula caused a decrease in 79 per cent of the tests; the average reduction in cardiac output was again 28 per cent. When the vagosympathetic trunks were sectioned and the fistula was occluded a decrease in cardiac output occurred in a comparable number of studies (74 per cent), the average decrease being 18.5 per cent. From Table I it will be observed that a decrease in cardiac output upon digital compression of the fistula occurred in 8 of 13 animals with normally innervated hearts (61.5 per cent), while the response was variable in one additional dog, making a decrease in output an invariable or occasional occurrence in 9 of the 13 (69 per cent). If those animals are excluded in which a significant rise in blood pressure did not occur upon occlusion of the fistula, a decrease in cardiac output was noted in 8 of 11 (73 per cent). In those dogs in which a sympathetic denervation had been performed a decrease in cardiac output occurred upon occlusion of the fistula in 7 of 10 (70 per cent) while one additional animal responded variably; thus a decrease occurred invariably or on occasion in 8 of 10 (80 per cent). If those animals are excluded in which a significant rise in blood pressure was not noted upon compression

of the fistula, a decrease in cardiac output was observed in 7 of the 8 animals (88 per cent). Such a response occurred on one but not both tests in the eighth dog studied. Following complete denervation of the heart a decrease in cardiac output upon occlusion of the fistula was observed in 9 of 14 animals (64 per cent) and a decrease was noted on occasions in 2 additional dogs; thus such a response occurred at times in 11 of the animals (78 per cent). If those dogs are excluded in which a significant rise in blood pressure was not observed during occlusion of the fistula, 7 of 11 animals exhibited a decrease in cardiac output (64 per cent) and a decrease occurred in one but not both tests performed upon another. Hence a decrease was noted invariably or on occasion in 8 to the 11 (73 per cent).

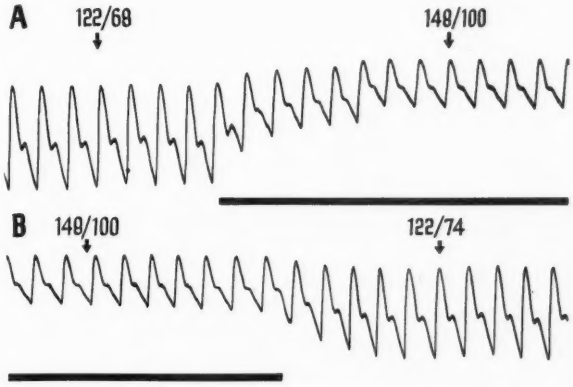

Fig. 4.—Optically recorded Hamilton manometer measurements of the change in blood pressure (*A*) upon occlusion and (*B*) upon release of pressure from the arteriovenous fistula in dog 3. The blood pressure rose from 122/68 to 148/100 with occlusion and upon release fell to 122/74. The pulse rate remained constant at 96 per minute. The period of occlusion is indicated by the heavy line. The record is actually a continuous one. At the time the study was made the complete extrinsic nerve supply to the heart had been interrupted.

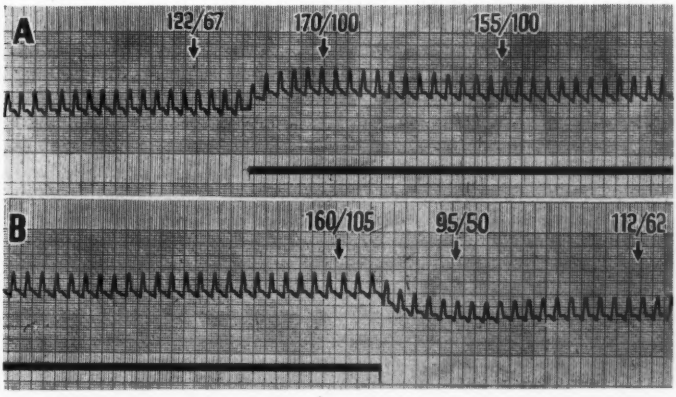

Fig. 5.—Electromanometric recording of alterations of blood pressure (*A*) upon occlusion and (*B*) upon release of compression of arteriovenous fistula in dog 15. The blood pressure rose from 122/67 to 170/100 upon occlusion, leveled off a few seconds later at 155/100, and then rose slightly to 160/105. Upon release of compression the blood pressure fell to 95/50 and quickly leveled off at 112/62. The pulse remained constant at 100. The period of occlusion is indicated by the heavy black line. The record is actually a continuous one. At the time this study was made the total extrinsic nerve supply to the heart had been interrupted.

Three and one-half months after the fistula was made, in the case of dog number 2, cardiac output was determined before and after digital occlusion of the fistula and then after exposure and precise ligation of the proximal vein. The output decreased from 4,400 c.c. per minute beforehand to 2,280 c.c. during digital occlusion. It was reduced to a comparable degree immediately after ligation of the proximal vein (2,660 c.c. per minute) even though there were present large venous collateral vessels and a strong continuous thrill persisted. Two months later the cardiac output had risen to the neighborhood of 5 liters per minute and digital occlusion brought about a striking reduction in output.

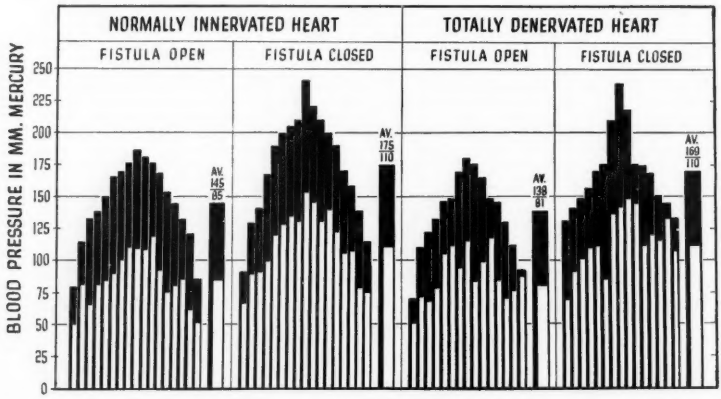

Fig. 6.—Values of systolic and diastolic blood pressure before and during occlusion of an arteriovenous fistula and in dogs with normal cardiac innervation and in dogs with total cardiac denervation.

There was a prompt rise in blood pressure upon occlusion of the fistula in 14 of the 17 animals studied and in 12 of them the elevation in pressure was marked. It is of some interest that of the 3 animals which did not exhibit this characteristic change in blood pressure, in 2 the proximal artery and vein connected with the fistula were observed to be thrombosed, even though the fistula was patent when examined after the animal was sacrificed, while our notes concerning the condition of the fistula at post-mortem examination were lost in the third instance. A rise in both systolic and diastolic pressure was noted. The change in blood pressure was repeatedly observed to occur with the very first beat of the heart after the fistula was compressed (Figs. 4 and 5). The peak of the elevation in blood pressure always occurred within 3 seconds after which it began to level off, reaching in approximately 20 seconds a plateau which remained considerably above the level observed before occlusion of the fistula (Fig. 4). In these figures is also illustrated the rapid reversal which takes place upon release of pressure from the fistula. The same type of change in blood pressure occurred regardless of whether the normal innervation of the heart was left undisturbed, whether its sympathetic fibers had been removed, or whether it had been totally denervated. In Fig. 6 are charted observations of alterations in blood pressure upon occlusion of the fistula in animals with normally innervated and totally denervated hearts. It can be seen that these changes are comparable in the two groups not only qualitatively but also quantitatively.

DISCUSSION

The studies reported would indicate that the characteristic decrease in cardiac output and elevation of blood pressure upon digital occlusion of a peripheral arteriovenous fistula take place regardless of whether the heart is normally

innervated, deprived of its sympathetic innervation, or totally denervated. The bradycardiac reaction observed in man does not occur in the dog asleep with pentobarbital. It is recognized that the method for estimation of cardiac output employed, though reasonably accurate, is nevertheless subject to some experimental error and that maintenance of the same basal status for all studies is difficult to achieve. It would be interesting to repeat these studies using another method for estimating cardiac output, for example, ballistocardiography. There can be no question about the accuracy of the blood pressure observations. Altogether, it would appear evident that the observations recorded constitute overwhelming evidence that the response of cardiac output and blood pressure follow the same pattern irrespective of the preservation or interruption of the extrinsic innervation of the heart.

We have assumed that removal of the sympathetic chain from above the caudal cervical ganglion down to below the fifth or sixth thoracic ganglion effectively interrupts all the sympathetic fibers to and from the heart. On gross examination we have not demonstrated any sympathetic fibers passing to the heart from any other portion of the sympathetic chain. Certainly this conclusion might be reached in man from the persistent bradycardia which follows extirpation of the chain from above the stellate ganglion to below the fourth or fifth thoracic ganglion, as well as from the relief of anginal pain when the same portion of the chain is removed. The interruption of vagal fibers in our studies was obviously complete. We have, of course, used the word total denervation in reference to the extrinsic nerve supply of the heart only.

Explanation of the prompt and dramatic decrease in output of the denervated heart upon occlusion of an arteriovenous fistula can be adequately accounted for according to the law propounded by Starling for control of the output of the heart. From studies of heart-lung preparations, he observed that the output of the heart was dependent solely upon the volume of input and was independent of the blood pressure against which the left ventricle must empty its load. His conclusion that the output was related to the input and more specifically to the degree of stretching of ventricular fibers has withstood the test of time. In the case of our experiments with complete extrinsic denervation of the heart of otherwise intact animals, the sequence of events can be explained as follows: The sudden occlusion of the fistula interrupts the immediate return to the heart of that relatively large volume of blood which has previously been returned directly from the fistula through the proximal vein. Thus, with the very next diastole of the heart, a reduced volume of blood enters the right atrium and subsequently the right ventricle. With the reduced input, the ventricular fibers are not stretched to the point which characterized the previous diastole and consequently a reduced volume is ejected with systole. Though the previous volume may still have passed into the left ventricle and been ejected from it with this first stroke, in the succeeding diastole the reduction is at play in left atrial and left ventricular input and the output necessarily becomes equal to the output from the right side. The reduced cardiac output continues to maintain a comparative reduction in filling and emptying of the heart. Some

idea of the significant reduction in the volume of blood returned to the heart immediately upon digital occlusion of an arteriovenous fistula is evident from other studies concerned with rotametric determination of the volume flow of blood through the proximal vein under various circumstances.[3] Blood flow values through the proximal vein have varied from 15 to approximately 75 c.c. per minute per kilogram of body weight, the average being in the neighborhood of from 30 to 35 c.c. per minute per kilogram. This flow is reduced to zero when the fistula is occluded digitally. It should be pointed out that the fistulas in this group were smaller than those in the animals used in the present study. It will be recalled that the values for total cardiac output in our animals with open arteriovenous fistulas averaged from a low of 223 c.c. per minute per kilogram in one group to a high of 302 c.c. per minute per kilogram in another. Furthermore, in at least one instance ligation of the proximal vein alone effected an immediate reduction in cardiac output of comparable degree to that brought about by digital occlusion of the fistula.

Other studies which we have carried out have not demonstrated any elevation above the normal range of right atrial pressure in dogs with open arteriovenous fistulas. Though the pressure in the femoral vein opposite the fistula is as high as arterial pressure, the pressure gradient rapidly falls and pressures are normal in the distal portion of the inferior vena cava. Moreover we have not demonstrated any significant alteration in right atrial pressure upon digital occlusion of the fistula.

The cardiac outputs in animals with open fistulas and complete interruption of the extrinsic cardiac nerve supply were not as high as in those with intact cardiac innervation or in those with sympathetically denervated hearts.* Explanation of this difference is not clear and further study of the problem is contemplated.

The elevation in blood pressure with occlusion of the fistula and its decrease with release of compression of the fistula may possibly be the result of the interplay of a number of factors, but it can be explained satisfactorily solely upon the sudden alteration in peripheral resistance. It is an interesting fact that the sudden occlusion of an arteriovenous fistula not only brings about a decrease in cardiac output but also an elevation in blood pressure. This means that the work done by the heart during the period immediately following compression of the fistula is not lowered in a degree comparable to the reduction in cardiac output. It is well known, however, that with passage of time after obliteration of a fistula the elevated blood pressure drops to a lower level and with this change would occur a diminution in the work load of the heart.

The demonstration that the characteristic response of cardiac output and blood pressure to the opening and closing of a peripheral arteriovenous fistula is essentially the same, regardless of the presence or absence of extrinsic cardiac innervation would lead one to believe that the response of the heart to other

*When the cardiac outputs in animals with open fistulas are compared statistically with those of normal dogs, the T score is found to be highly significant in the group with intact cardiac nerves, in that with sympathetically denervated hearts, but not definitely significant in that with totally denervated hearts. Yet in approximately 75 per cent of each of these 3 groups a decrease in cardiac output occurred upon digital compression of the fistula.

changing stresses may also be more dependent upon mechanical factors than upon extrinsic nervous regulation. We have been impressed with the importance of initiating other experiments designed to elucidate this and related problems.

SUMMARY AND CONCLUSIONS

1. Studies are reported demonstrating that the characteristic decrease in cardiac output and increase in blood pressure upon digital occlusion of an arteriovenous fistula take place in dogs with sympathetically denervated hearts and in dogs with total interruption of their extrinsic cardiac nerves as well as in animals with normally innervated hearts.

2. The change in cardiac output upon opening or closing an arteriovenous fistula is explained according to Starling's law upon alteration in the volume input and consequent differences in the stretching of the ventricular muscle fibers. The change in blood pressure would appear to be explainable upon the alterations in peripheral resistance.

The authors wish to express their appreciation to Dr. N. N. Stahl and Dr. E. E. Wayson for their help with the initial studies performed.

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EXPERIENCES WITH THE EXPERIMENTAL SURGICAL RELIEF OF AORTIC STENOSIS

A Preliminary Report

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THE therapeutic problems posed by the presence of chronic valvular disease of the heart have alternately stimulated and baffled the combined ingenuity and daring of both physician and surgeon for many years. The possibility of a direct surgical approach has been particularly intriguing to the surgeon, especially when the valve has become stenotic in character. As stenosis is essentially a mechanical stricture, its relief must logically be sought by mechanical (surgical) means. Undoubtedly struck by a similar conclusion, Tuffier,[1] in 1914, successfully attempted surgical relief of a stenotic aortic valve. The patient was a young man who had shown signs of a marked and progressive aortic stenosis. The thorax was opened and the root of the aorta exposed. It was the operator's intention to insert a knife above the aortic ring and to incise the stenosed valve, but the procedure was changed to a dilatation of the aortic valve by invaginating the wall of the aorta just above the valve and pushing its wall into the stenosis on the forefinger. As late as 1924, this patient was reported living and improved. To date no other definitive surgery upon the human aortic valve has been reported.

Emboldened by a reasonable measure of success with the surgical alleviation of mitral stenosis, it was natural that attention should be turned toward its counterpart in the aortic valve. Our interest in this phase of valvular surgery was initiated by the enthusiasm and efforts of the late Horace Smithy, whose untimely death resulted from the rapid devastation of the disease under discussion. It became apparent at once that the lessons learned and the approaches employed in the development of mitral surgery could not be transposed in toto to the aortic valve because of the latter's variation in anatomic structure and relationships to vital coronary pathways. Nevertheless, certain broad patterns for investigation suggested themselves as a result of experiences encountered in this earlier experimental and clinical phase of valvular surgery.

PATHOLOGIC AND PHYSIOLOGIC CONSIDERATIONS

The pathology of aortic stenosis is varied and complex. It appears that the primary defect in the rheumatic type is an early fusion of the valve cusp margins. The free edges of the valve cusps are thickened, rolled, and eburnated.

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They may actually contain calcium but even in its absence are extremely hard and tough. The valve leaflets themselves vary greatly but are invariably thickened and in most fixed specimens appear rigid and unyielding. In extreme cases the entire aortic valve may be considered as a rigid orifice surrounded by a calcified plaque having lost all semblance of its original tricuspid nature. The fresh specimen, however, frequently reveals a considerable amount of flexibility of the cusps themselves, especially near their attachments to the aortic wall. In this respect the pathology resembles that found in the average case of mitral stenosis (Figs. 1 and 2).

Stenosis of the valve thus described does not seem actually to involve the aortic wall itself. Bell[2] has pointed out that intimal atherosclerotic changes of the ascending aorta are invariably absent in these cases. He feels that the so-called degenerative aortic stenosis is actually only a late form of the initial rheumatic lesion in which calcium deposition plays a prominent role. He has demonstrated in a large autopsy series numerous transition stages between undoubted rheumatic and calcific stenosis. Associated mitral disease, myocardial Aschoff bodies, and other rheumatic stigmas are practically the rule in carefully investigated cases of "degenerative" aortic stenosis. Thus available evidence supports the rheumatic origin of nearly all cases of this disease. Even in clear-cut rheumatic cases calcification is common. It may merely thicken and indurate the valve edges and the cusps themselves, or it may extend down one or more commissures (fused valve edges) into the immediately adjacent aortic wall. In some cases it then extends as a long stalagmite of limestone nearly free in the aortic lumen except for its lateral attachment. The orifices of the coronary arteries are located approximately one centimeter above the two anterior valve cusps. Rarely, if ever, do they become involved or distorted by the disease process originating within the valve (Figs. 3 and 4).

The disturbed physiology in extreme aortic stenosis is apparently due to the slow ejection of a relatively small amount of blood with each contraction of the left ventricle. As a result the systolic blood pressure does not reach high levels but is sustained and maintained longer than is usual. Diastolic pressures likewise are relatively high, so that the pulse pressure differential is small. Coronary flow is probably reduced more by the diminished volume of blood in the aorta than it is by either pressure changes or intrinsic disease in the coronary system itself. Naturally, the coronary vascular needs of the left ventricle are increased by virtue of the large bulk of musculature contracting partly isometrically against the aortic obstruction. This extra work load increases the relative inadequacy of the coronary flow and thus probably explains the "anginoid" or "coronary" type of pain so often seen in these cases.

Patients with uncomplicated aortic stenosis are not dyspneic unless congestive failure has supervened. They become progressively disabled as their cardiac stroke output diminishes with increasing stenosis. Eventually even the slightest exertion produces dizziness and fainting. Persistence in exertional efforts leads to greater discrepancy between supply and demand, both sys-

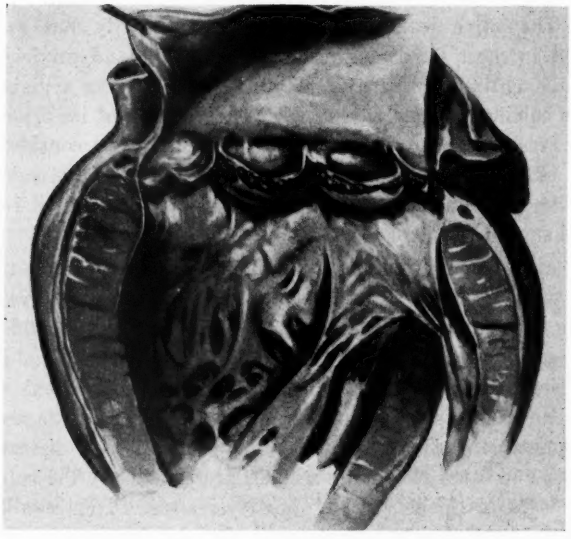


Fig. 1.—Rheumatic vegetations on free edges of aortic valve cusps.

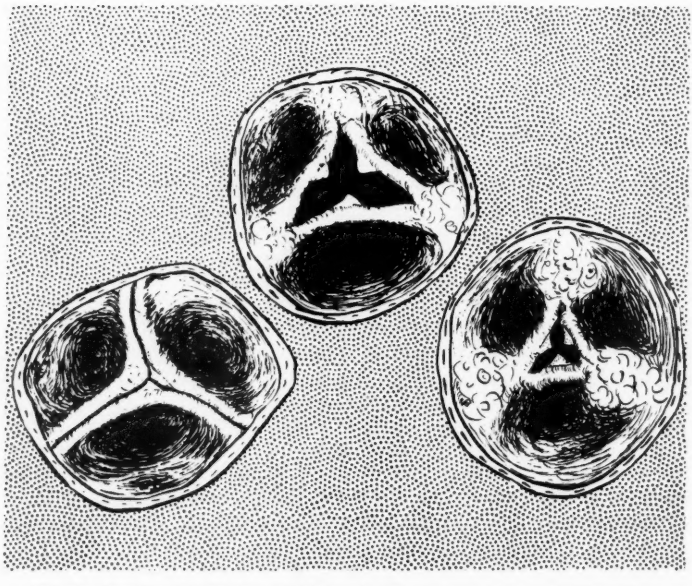


Fig. 2.—Progressive fusion of adjacent valve cusps at the commissures.

temically and with regard to coronary flow. In all probability this may explain the relative frequency of sudden death which so often follows rather moderate effort in cases with this type of lesion.

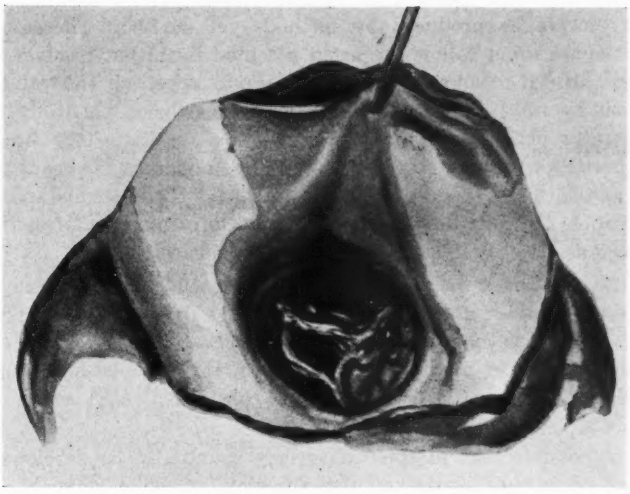


Fig. 3.—Typical and basic pathology of aortic stenosis.

Fig. 4.—Extreme anatomic distortion of aortic valve by fibrosis and calcification. Even here considerable flexibility is usually observed in the fresh specimen.

EXPERIMENTAL CONSIDERATIONS

The approach to the problems of stenotic valvular disease in the experimental laboratory is fraught with many difficulties. The experimental animal does not have valvular stenosis, nor can a reasonable facsimile of the human pathologic picture be produced by methods yet devised. Therefore, animal experimentation cannot follow the usual accepted form, but resolves itself into methods of surgical technique designed either to approach the valve itself or to by-pass it by involved methods of vascular anastomoses. Study of human heart specimens obtained at autopsy is likewise unsatisfactory because they usually represent extreme states of disease—a distortion of the conditions which may exist at the time when surgery could reasonably be contemplated. Further, because fixation of the tissues has destroyed certain important functional components such as mobility, bizarre conclusions are drawn.

The first reaction of the authors following a study of preserved specimens of aortic stenosis was that only an entirely new valve could offer a reasonable solution. The obvious conclusion to such an observation lay in three directions: (1) the insertion of a mechanical valve or (2) the replacement or (3) by-passing of the damaged valve by a section of transplanted aorta containing normal valves.

1. It is possible that plastic valves may eventually be developed for the replacement of normal aortic valvular function. Such a valve has been employed experimentally by Hufnagel[3] and Campbell.[4] Whether this valve or others embodying the same principle will be satisfactory is open to question. They are inserted into the aorta beyond the coronary ostia, thus violating the normal relationship between valve and coronary. Normally, with a competent valve, coronary flow is maintained by the head of pressure within the aorta during ventricular diastole. The physiologic effects of this reversal of position will require intensive study, but would seem to be a serious objection to this type of approach.

We have had no experience with prosthetic valves. Our initial experimental attempts, however, employed a somewhat similar principle using homologous body tissues. The concept was to excise a portion of stenotic valve and replace valve action by an inverted vein graft similar to the technique used by Murray[5] in mitral valve surgery.

Using mongrel dogs, the external jugular vein was removed and turned inside out to present an endothelial surface to the blood stream. A segment of tendon was then passed through the inverted vein to lend it substance. A specially prepared cork borer was then passed through both aortic walls near its root at the myocardium. The prepared vein graft was drawn through the lumen of the borer, which was then withdrawn, leaving the graft transfixing the aorta. Purse-string sutures in the aortic wall prevented bleeding about the openings. However, the great depth of the aortic valve within the heart substance required such a long graft loop that efficient valvular function and diastolic tamponade was not obtained. Attempts to insert the graft within the myocardial portion of the aorta failed because of the proximity of the coronary vessels (Figs. 5, 6, and 7).

2. Direct valve grafts using small segments of aorta and pulmonary artery with their contained valves met with a similar fate, primarily from massive hemorrhage. One animal survived the procedure and the valve graft became intimately attached to the aortic ring. However, the valve did not function be-

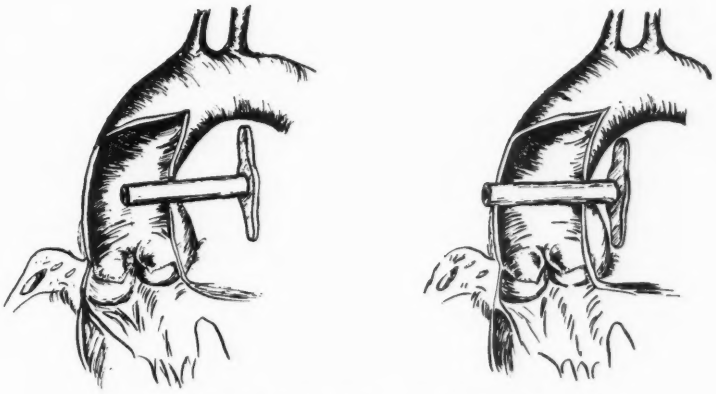


Fig. 5.—Passage of cork borer through both aortic walls.

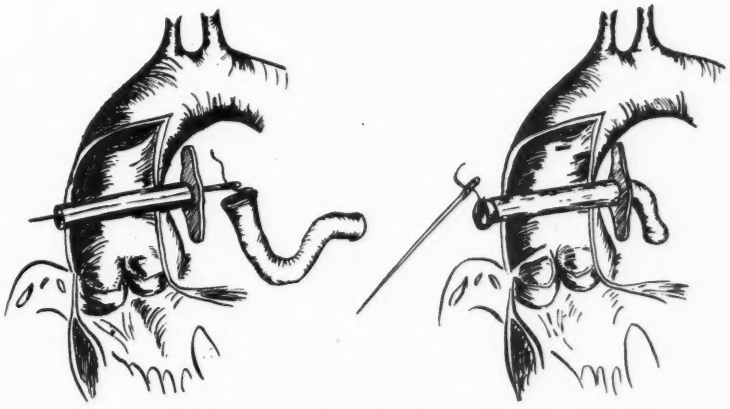


Fig. 6.—Passage of inverted vein graft through cork borer.

cause of distortion of its cusps. The great dangers associated with these maneuvers led us to discard, at least temporarily, this idea of direct valve transplantation.

3. A. Methods of by-passing the aortic valve using free grafts of aorta were then explored, utilizing two methods of approach to the left ventricle. First the aortic valve, aortic arch, and descending thoracic aorta were removed en masse from sacrificed dogs. All tributary vessels along the course of the aortas so obtained were ligated. The aorta was then divided into two separate

grafts by severing its continuity just below the left bracheocephalic artery. The distal end of the valve-bearing graft was then anastomosed by end-to-side technique to the descending aorta using the Potts-Smith aortic clamp method. After release of the aortic clamp the grafts became distended with blood and pulsated. The three transparent valve cusps approximate perfectly and restrain blood flow without leakage. The other graft segment from the descending aorta was then anastomosed end-to-end to the valve-bearing end of the pulsating graft, thereby obtaining additional length toward the left ventricle.

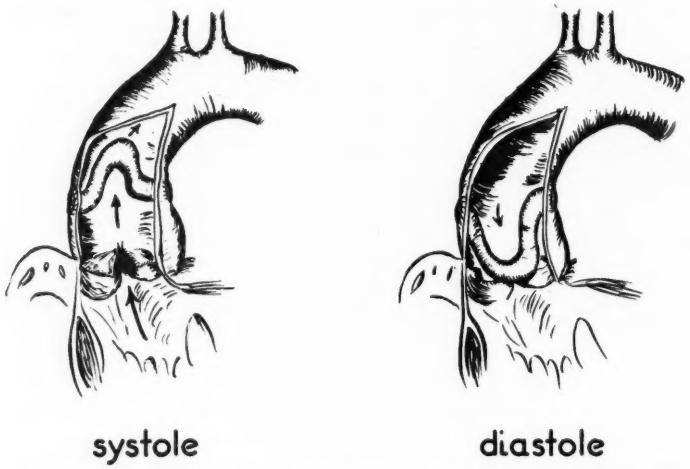


Fig. 7.—Movement of vein graft. Tamponade of valvular defect during diastole.

A site for insertion of the free end into the left ventricular cavity was then selected at a point away from the coronary vessels, mitral valve, and its papillary system. The free end of the graft was inserted into the left ventricle through a stab wound using four silk sutures fastened to the quadrants of the graft. These sutures were passed from within the ventricular lumen outward through the cardiac wall. Hemorrhage between graft and myocardium was controlled by purse-string suture in the myocardium and interrupted sutures as needed.

This technique was attended by an excessive operative mortality from hemorrhage, ventricular fibrillation, and mitral insufficiency due to the inclusion of chordae tendineae in the sutures. In addition, essential hemostatic purse stringing in the myocardium may partially or completely occlude the orifice of the graft within the left ventricle. Of eight dogs subjected to this technique, only one survived more than a few days.

B. An improvement in the technique consisted in using a somewhat longer portion of the descending aorta for the graft. This portion of the graft could then be passed through a cylinder of Polythene of appropriate size and long enough to extend completely through the ventricular wall. The free end of the graft was then drawn back over the Polythene to form an endothelialized cuff

completely over the tube. Because of the rigidity of this portion of the prepared graft, it was easy to insert into the ventricular lumen, and more adequately to control bleeding by simple tightening of the myocardial purse string. Simple suturing of epicardium and graft was sufficient to securely hold it in place (Figs. 8, 9, and 10).

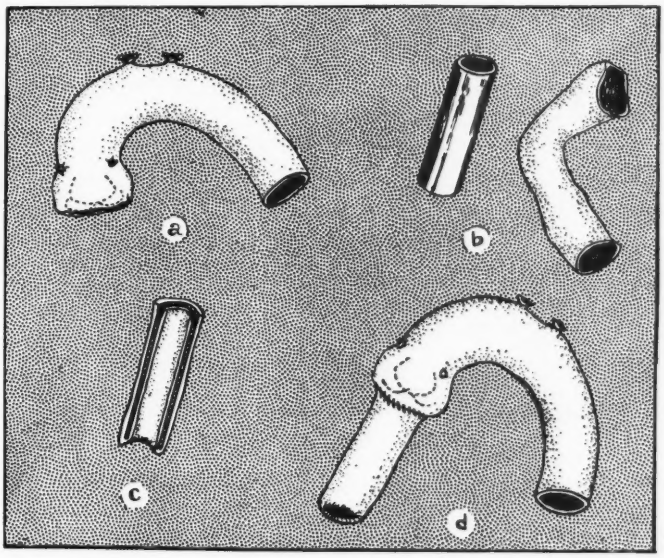


Fig. 8.—Preparation of double aortic graft including the aortic valve and incorporating a cylinder of Polythene in its proximal segment.

While this technique was superior in that hemorrhage was better controlled, in that obliteration of its lumen could not take place, and in that no great quadrant sutures were necessary to draw the graft into the ventricle, thus protecting the coronaries and chordae tendineae, not one of our twelve dogs survived. It appeared that the deaths were not due to the actual surgical maneuvers but to some grave physiologic disturbance produced by the by-pass. There was no doubt that the shunt functioned as shown by clamping it distally and incising it just proximal to the clamp. Whether the double ventricular outlet provided too easy escape of the ventricular output, thus relieving the muscular work load, or whether by-passing the coronary mouths in some way impaired myocardial function, the hearts slowed down, became feeble, and soon ceased to contract, immediately after removing a clamp placed across the middle of the graft. Prompt replacement of this clamp permitted some of the animals to improve but every time it was removed the phenomenon of the failing heart was repeated.

It is conceivable that the human heart with clinical aortic stenosis might better withstand the establishment of a second aortic outflow tract, but on the basis of these results obviously clinical trial was out of the question.

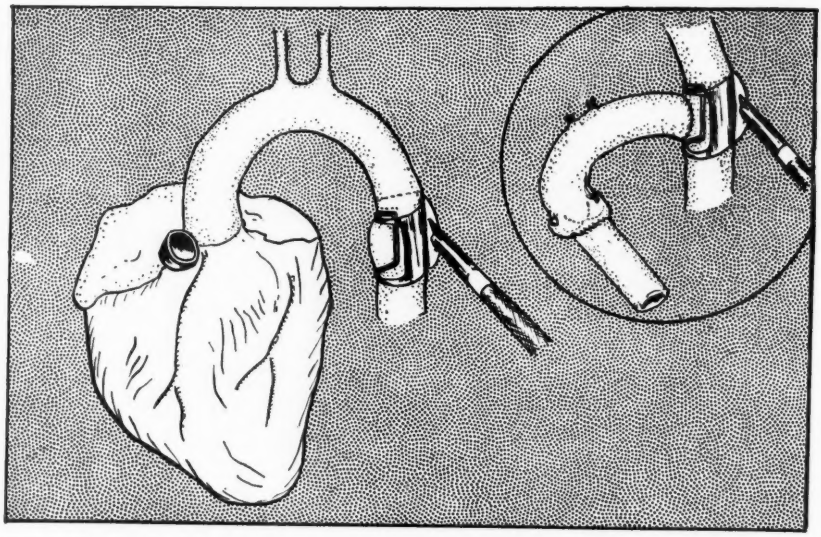


Fig. 9.—Anastomosis of distal end of graft to descending aorta using the Potts-Smith clamp and technique.

Fig. 10.—*A*, Proximal end of graft inserted directly through the left ventricular wall. *B*, Proximal end of graft inserted through left auricular appendage, left atrium, and mitral valve, to enter the left ventricular chamber.

C. It did occur to us, however, that the heart might be better able to tolerate a second aortic outflow tract if less major insult were made upon the myocardium itself. From our experiences with mitral valve surgery using the left auricular appendage to approach first the auricle, then the valve, and then actually to insert a finger and instrument into the left ventricle, we felt that a somewhat longer graft incorporating a longer tube of Polythene might well be inserted into the left ventricle by this route. The flexible mobile normal mitral valve cone would be large enough to permit insertion of a fairly large tube and would accurately close and grip it during ventricular systole, much as it grips the exploring finger. Therefore, longer grafts were prepared, and the free ends were inserted into the left ventricle via the auricle. There was no technical difficulty in seven dogs so operated. All survived at least twenty-four hours. However, a good flow through the graft such as obtained when the direct ventricular route was used was only intermittently obtained. It appeared that the ventricular wall or septum would encroach upon and intermittently occlude the orifice of the tube. In spite of the use of curved tubes and tubes with lateral openings, reliable constant blood flow through the graft was not obtainable. This may have been the reason the double aorta was better tolerated by this technique than by the direct ventricular approach. The smaller size of the distal end of the tube, necessitated by the limited size of the mitral orifice and by the smaller lumen of the lower aorta, would also tend to limit the physiologic disturbances due to a double ventricular output.

However, there was an observed tendency to sudden death among these animals while apparently in satisfactory health even several weeks after surgery. Autopsy disclosed complete thrombosis of the tube in all but one of the animals, but no other clear-cut cause of death. We presumed that the rigid tube lying in the ventricular chamber in close approximation to the septum was able to stimulate and produce various arrhythmias, eventually culminating in sudden death.

Discouraged by these attempts at by-passing or replacing the aortic valve, our efforts were redirected toward punch resection of the aortic valve. It was possible to pass a backward-cutting punch through the left ventricle up through the aortic valve, and to engage and remove a piece of the valve. In each case a typical thrill of aortic regurgitation was produced, accompanied by visible enlargement of the ventricle. Four dogs treated in this fashion survived the procedure but twelve died within twenty-four hours. When examined, a good sized defect of one of the cusps was evident in each case. However, we were impressed by the complete destruction of that cusp and questioned whether the technique would be applicable clinically. Certainly a high grade of aortic regurgitation would be a most undesirable result in human surgery.

Approach to the aortic valve by way of the innominate artery (brachiocephalic in dogs) is quite feasible. A forward-cutting punch of suitable size can readily duplicate the procedure performed through the ventricle. Six dogs were subjected to this procedure with one death. Again the amount of regurgitation produced by this method was most impressive and suggestive of its inapplicability to human cases (Figs. 11 and 12).

Smithy and Parker[6] apparently deemed an approximately equivalent amount of regurgitation produced by a hooklike instrument inserted through either the aortic or ventricular wall to be acceptable even in human patients. Of this we have grave doubt. They felt that the ventricular approach was preferable because of greater ease in controlling hemorrhage and in performing vascular repair than possible by the aortic approach. We believe that the innominate (bracheocephalic) artery is preferable to either, and even more readily controlled and repaired. We were unwilling to accept the idea of punch excision of the valve in a human patient, basing our objections in part on the following line of reasoning.

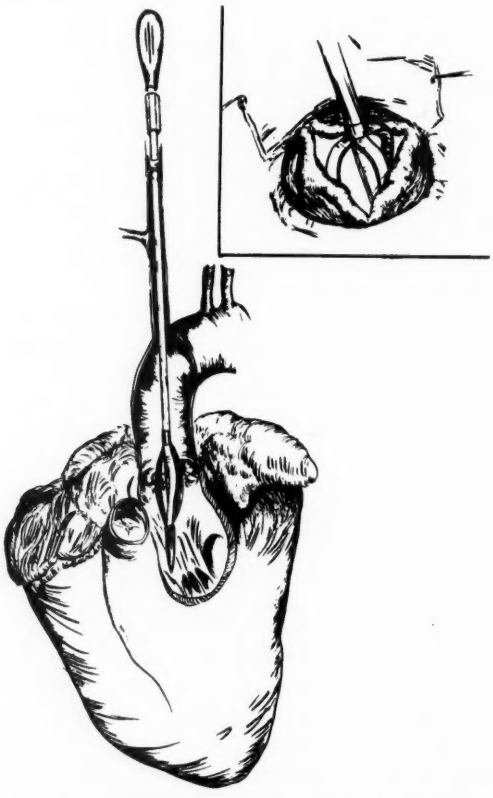


Fig. 11.—Simple incision of aortic valve cusp by innominate approach. Inset shows probable effect upon a stenotic valve.

In human aortic stenosis the lumenal passage through the valve becomes reduced, eventually to a small triangular or irregular central opening unable to open or close completely in any phase of the cardiac cycle. Regurgitation is therefore an inherent minor component of true stenosis. However, some stenotic

valves are seen in which considerable motion of the edges of the aortic slit does seem possible. Such valves present even more difficulty in attempts at direct surgical correction, since having had no pre-existing regurgitation and having an enormously hypertrophied left ventricular wall with a lumenal capacity reduced below normal, they are poorly equipped to compensate for any aortic regurgitation which might be suddenly produced during surgery. Certainly

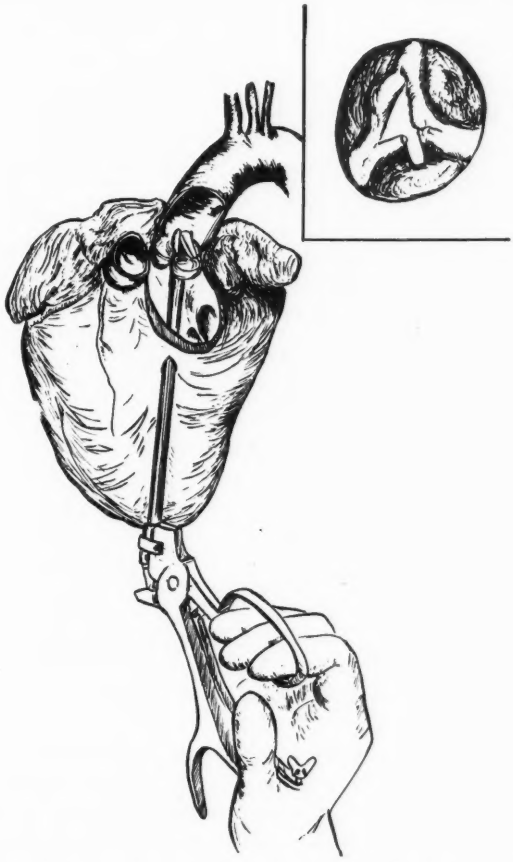


Fig. 12.—Resection of portion of valve cusp using backward cutting punch and the ventricular approach. Only four of sixteen dogs so operated survived. Each of these four exhibited remarkable and prompt dilatation of the left ventricle. This dilatation was effectively compensatory for the suddenly produced regurgitation.

regurgitation can only be compensated for by dilatation of the left ventricular chamber sufficient to expel at each contraction an amount of blood equal to that necessary for the maintenance of an adequate circulation plus the amount lost from the aorta by regurgitation through the valve. The tremendous hypertrophy of the myocardial musculature seen in clinical aortic stenosis would not seem to readily lend itself to such rapid and extreme dilatation.

Recently we have become familiar with the Brock technique for direct division of the pulmonic valve in congenital stenosis.[7] We have used the direct technique in six cases of cyanotic heart disease with excellent results. In pulmonic valve stenosis the three cusps of the valve have apparently become agglutinated or fused during fetal life into a valve cone with a tiny orifice at its apex. Only a trickle of blood can pass into the pulmonary circulation. Usually another defect exists to shunt the right ventricular blood into the systemic

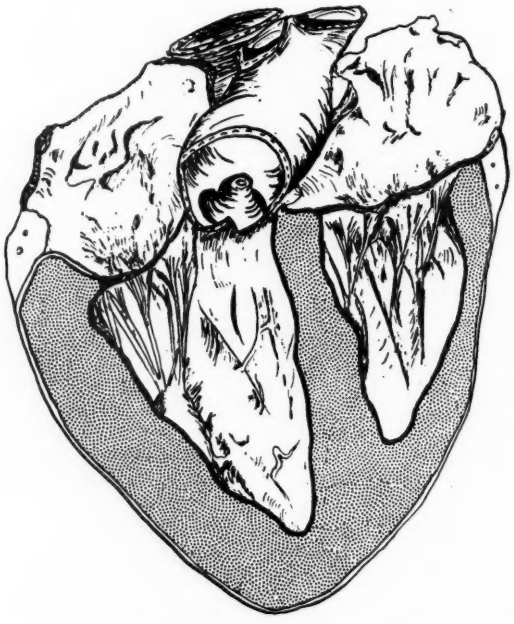


Fig. 13.—Typical pathology of congenital stenosis of the pulmonary valve.

circulation. Brock passes a flat diamond-shaped knife through an incision in the right ventricular wall, through the stenotic valve, dividing it into two halves. In other words, the valve cone formed by fusion of the three valve cusps is divided into a bicuspid valve. Pulmonary valves are occasionally naturally bicuspid and function without evident regurgitation. Postoperatively we have been unable to detect regurgitation in our cases, and Brock does not mention it (Figs. 13, 14, and 15).

Since the pulmonary and aortic valves are similar in construction and in method of action, we conceived the idea of performing a comparable operation for aortic stenosis. If we could produce a bicuspid aortic valve in spite of fibrosis and calcification, we felt that the strong left ventricle would force it open during systole, and that its very rigidity would prevent regurgitation

during diastole. There were, however, certain important extra considerations necessary in comparable surgery within the left ventricle.

First, it seemed unbelievable that life could be maintained more than a few seconds if an incision were made in the left ventricle comparable in size to that used in the right. Therefore, we constructed an instrument with a suitable curve, $\frac{3}{16}$" in diameter, with retractable diamond-shaped cutting blades near its apex. It required only a tiny puncture wound for insertion through the ventricular wall (Fig. 16).

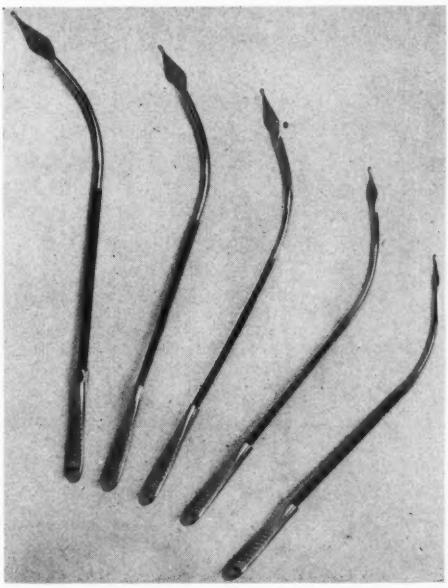


Fig. 14.—Brock-type flat valvulotomes.

Second, the presence of the coronary ostia just above the two anterior aortic valve cusps suggested a possible danger. If any inadvertent regurgitation were to be produced by surgery, it would probably be preferable that it take place through the posterior cusp. Otherwise, the rapid flow of regurgitating blood past one or other coronary orifice would markedly interfere with coronary flow during the normal diastolic filling period. Therefore, the retractable blades were placed in such a manner as to cut vertically rather than horizontally as in the Brock technique. Many specimens of aortic stenosis were studied to permit the instrument to be placed so that the upper blade would cut open the anterior commissure, or zone of fusion of the two anterior (coronary bearing) aortic cusps. The posterior blade would then cut across the center of the posterior (noncoronary) cusp. The valve should then be divided into an essentially bicuspid valve (Fig. 17).

CASE REPORT

After employing this technique on several dogs and cadavers merely for orientation, we felt that the method was applicable clinically. Therefore, on March 9, 1950, at the Episcopal Hospital, F. B., a 26-year-old white woman, unable to climb four steps without extreme dizziness, was subjected to operation. She had suffered from anginal pain even at rest for over a year. Blood pressure averaged 96/88. Pulse was regular at 80 per minute. She had a typical systolic aortic murmur and thrill and moderate cardiac enlargement.

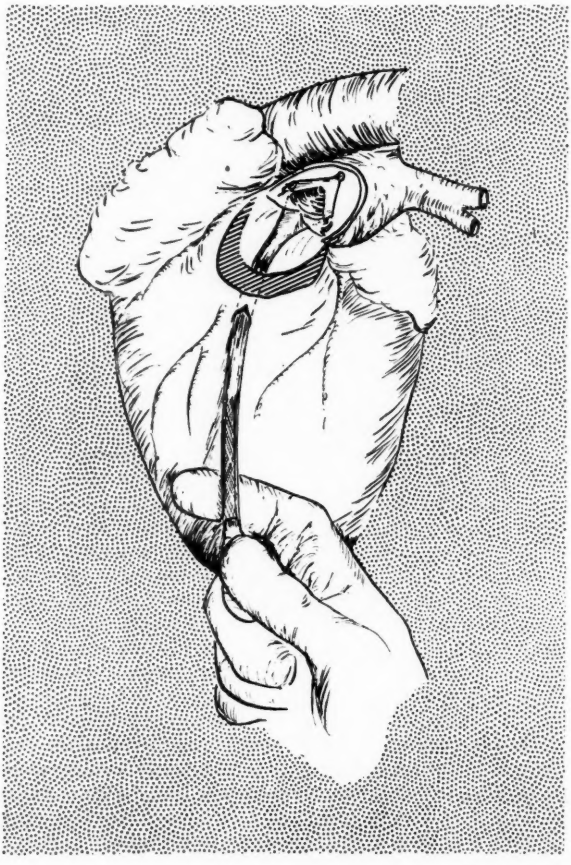


Fig. 15.—Division of stenotic valve cone into bicuspid pulmonary valve. Such bicuspid valves do not exhibit marked regurgitation.

With the patient in the supine position, the usual left inframammary incision was made. The thorax was entered through the fourth left interspace. Ribs four and five were spread and the costal cartilages were divided. The pericardium was widely opened anterior to the left phrenic nerve after flooding it with 5 per cent procaine. The point of the myocardium selected for insertion of the special retractable knife was infiltrated with 0.5 per cent procaine.

A purse-string suture and two mattress-stay sutures were placed about the selected point—1 inch above the ventricular apex and ¾ inch to the left of the anterior descending coronary artery. A small stab wound was made and the medium-sized retractable knife was inserted into the ventricular lumen. It was gradually passed up along the ventricular septum to the

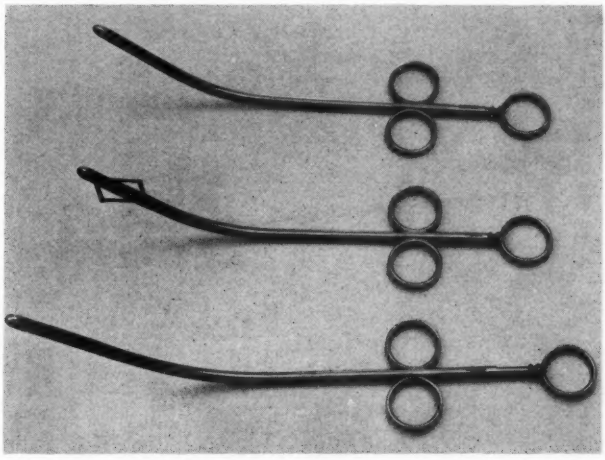


Fig. 16.—Special valvulotomes with retractable blades for anteroposterior division of fused aortic valve.

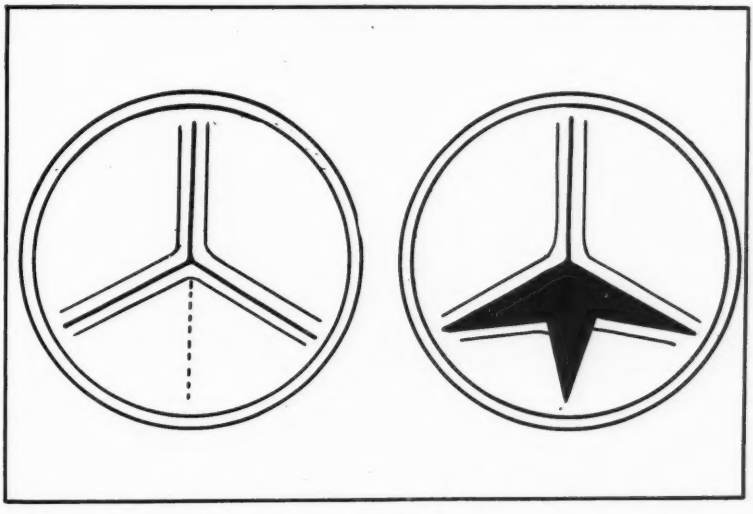


Fig. 17.—Proposed line of division of aortic valve—through the commissure between the two anterior or coronary bearing cusps and across the posterior cusp.

region of the aortic valve. Soon the calcified areas of the valve were palpable by the instrument, but the lumenal opening appeared to be most difficult to find and enter. After many unsuccessful attempts to pass the instrument through the valve, the patient's condition seemed unsatisfactory and the instrument was withdrawn to permit the heart to rest. Bleeding was controlled with difficulty because the myocardium seemed to be very friable and unsuitable for tying of sutures. However, the very thick myocardium soon stopped the bleeding spontaneously.

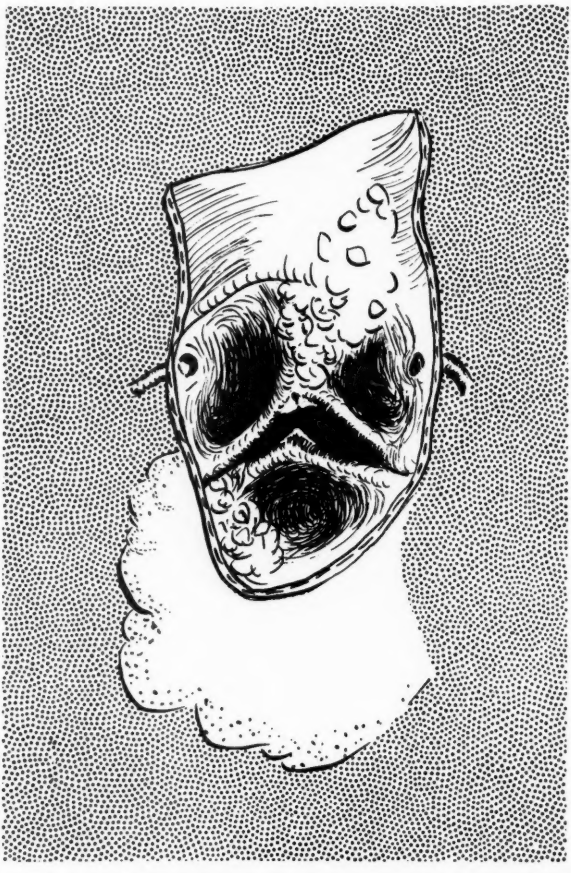


Fig. 18.—Actual pathology existing in human case at the time of surgery. Note heavy calcification in the region of the anterior commissure.

Strong cardiac contractions returned, and we considered other methods of resolving the problem. One of the difficulties in aortic surgery is the inability to see readily the diseased valve, either by direct vision or by the tactile or "digital" vision which we have employed in surgery of the mitral valve. However, both in dogs and in human beings it is sometimes possible to feel the aortic valve momentarily by the "Ramirez maneuver." With the patient supine, the surgeon stands on the right side of the table and inserts his left index finger

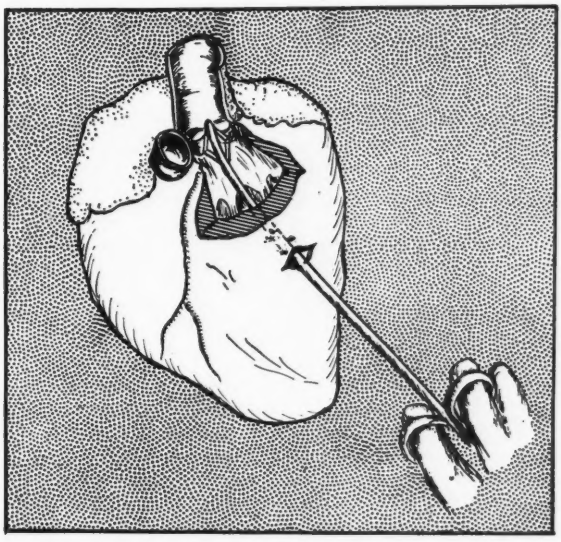


Fig. 19.—Division of human aortic valve.

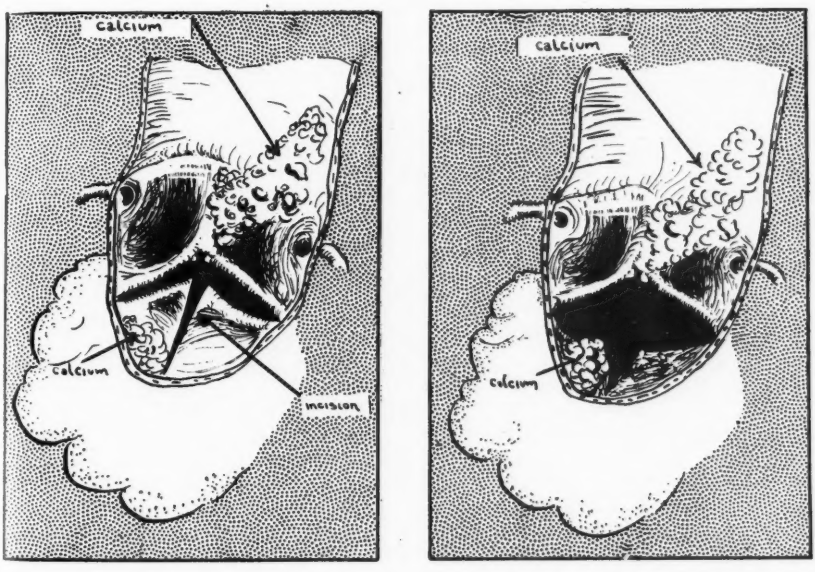


Fig. 20.—Actual line of division of human aortic valve. The calcified anterior commissure was only slightly cut. The posterior leaflet was divided.

through an incision in the left auricular appendage. The finger is then passed through the mitral valve and is bent back sharply to palpate the aortic valve. It is conceivable that actual digital dilatation of the aortic valve could be carried out in this manner.

Fig. 21.—Ventricular aspect of divided aortic valve.

Fig. 22.—Showing regurgitant effect of division of this same valve which manifested a surprising amount of flexibility.

An attempt was made to perform this maneuver. However, the left auricular appendage in this individual with no mitral valve disease was too small to permit the index finger to enter the auricle beyond the first joint. On the other hand, had there been mitral disease the auricular appendage would have been large, but the narrowed mitral orifice would scarcely have permitted the insertion of a finger into the ventricle without severe obstruction of the auriculoventricular blood flow.

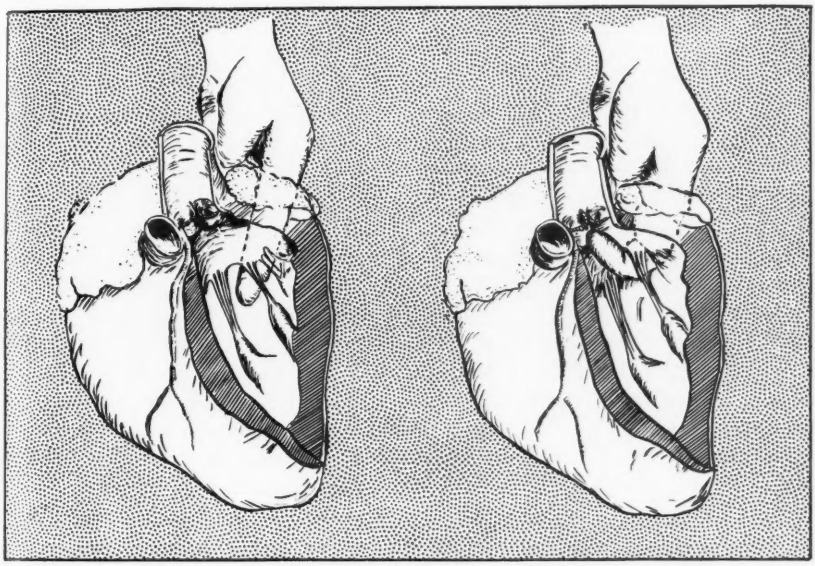


Fig. 23.—Ramirez maneuver for palpation of the aortic valve. The finger is inserted through the mitral valve via the left atrium and appendage.

After closing the auricular appendage it was determined that another attempt should be made to cut the aortic valve by the modified Brock method. The instrument was again inserted into the left ventricle and after some probing passed up into the aorta. The retractable blades were opened and the valve was cut by pulling the instrument back into the ventricle. Great resistance was met, but the instrument was finally pulled through in a partially opened position. Immediately the heart became slow and began to fail. The instrument was withdrawn and the myocardial defect rapidly sutured. In spite of stimulation, rapid transfusion, and prolonged cardiac massage, only a very transient heartbeat could be re-established. It was notable that in the dying state the left ventricle did not become dilated although the other chambers rapidly became enormous. Perhaps this inability of the left ventricle to dilate because of its great muscular hypertrophy is responsible for the frequency of sudden death in cases of aortic stenosis.

Autopsy revealed that the knife had been well placed. The anterior blade had engaged accurately upon the anterior, unfortunately calcified, commissure and had penetrated 3/16 inch through pure calcium. The posterior blade had cut directly across the middle of the posterior cusp for 1/4 inch completely dividing the hard eburnated edge. It was evident from the specimen that appreciable regurgitation had been produced by division of this cusp. An amount of regurgitation far less than that tolerated by healthy dogs had been incompatible with life when superimposed upon diseased tissues (Figs. 18 to 23).

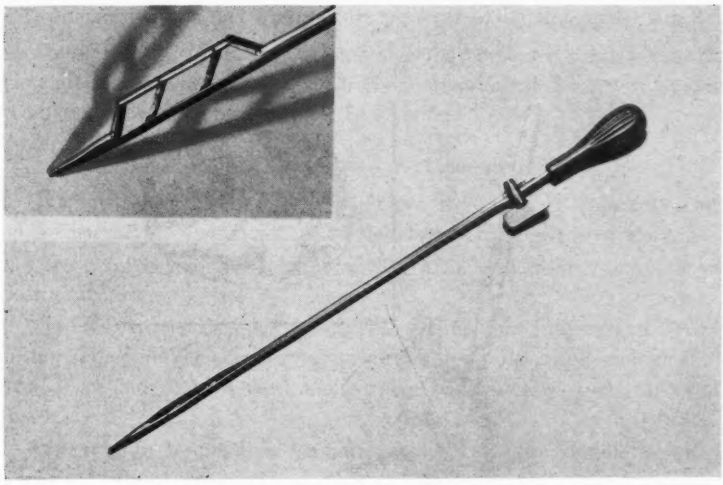
The idea of creating in effect a bicuspid aortic valve without producing regurgitation at least in this instance seemed untenable. The fresh heart specimen revealed only an average amount of pathologic change when compared with fixed specimens. The valve displayed a considerable degree of flexible though thickened, tissue in two of the cusps and at two of the fused commissures. Because of this flexibility the interruption of the hard posterior valve edge presumably led to immediate fatal regurgitation. Division of the fixed specimens with their artificially hardened cusps had not suggested the probability of regurgitation.

Shocked and saddened by this turn of events, we have abandoned the idea of further attempts at cutting the valve for the time being. It would be eminently desirable to cut accurately the fused commissures of the stenotic valve, but this can only be done under clear vision. None of the various artificial heart-lung extracorporeal systems has as yet been perfected sufficiently to permit exclusion of the human heart from the circulation. Cardioscopic or other means of direct visualization are not yet feasible during surgery of the aortic valve.

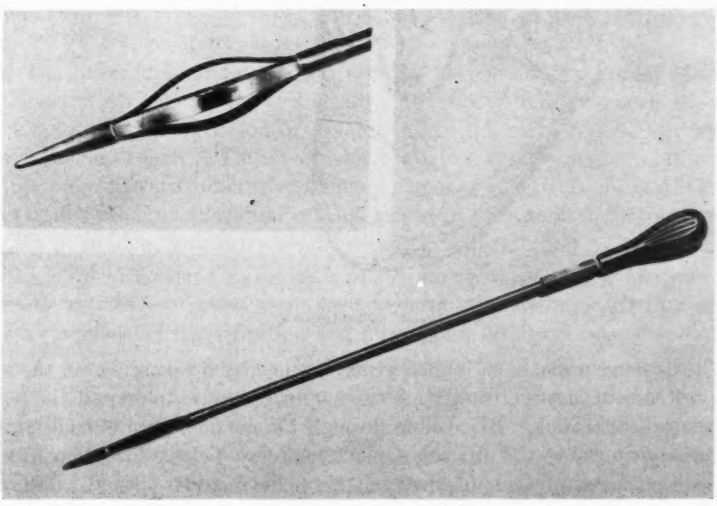
In the meantime we have channeled our efforts in another direction. Digital dilatation of the mitral valve is not without value in the treatment of mitral stenosis. Indeed, the first truly successful effort at the treatment of mitral stenosis made by Souttar, in 1925,[8] was a simple digital dilatation using the auricular approach. More recently Brock, as well as the authors, has occasionally performed digital dilatation alone for mitral stenosis. The difficulty is that tearing will occur in the line of least resistance, which may or may not be in a favorable location. The mitral valve with heavy calcified lips invariably tears at one or both commissures, producing in effect a planned commissurotomy, but as a rule limited by the size of the dilating finger. On the other hand, the valve which is not calcified, not greatly indurated, but merely closed at its orifice as though by a draw string will usually tear across the thinner anterior lip. Thus, a patient ideal for simple lateral commissurotomy must die from uncontrollable regurgitation. We have demonstrated this mechanism both in the pathology laboratory with fresh specimens, and also to our sorrow in a living operated patient.[9, 10]

However, the aortic valve in serious acquired clinical stenosis appears to have no exact pathologic counterpart to this "purse-stringed" state. Indeed, the free edge of the cusp in aortic stenosis appears to bear the brunt of the disease process. It is thickened, indurated, and tough. It is often ossified. By simple forceful dilatation of the stenotic aortic valve in the laboratory it is possible to tear open one or more of the sealed commissures without injury to the valve cusp itself. Such an opening of the valve should produce little if any additional regurgitation, since the cusp as a whole will function better after mobilization. True, it would be unusual for all three commissures to tear open with restoration of essentially normal valve function. However, the powerful hypertrophied left ventricle, able as it is to compensate until veritably only a trickle of blood can pass the aortic barrier, will readily respond to even moderate relief of the obstruction.

We have therefore devised an instrument shaped like a large pencil with a blunt point. This is inserted through an incision in the neck into the lumen of the right common carotid artery. It is gently guided through the innominate artery into the ascending aorta, and soon impinges upon the aortic valve. This is readily recognized both by resistance to further passage and by the direct



A.



B.

Fig. 24.—*A*, Aortic dilator with single dilating arm. *B*, Aortic dilator with triple dilating mechanism.

transmission of the cardiac movements to the operator's hand through the instrument. The instrument is then withdrawn about two centimeters, redirected slightly, and propelled forward with fingertip touch. After a number of such attempts the instrument will engage within the narrowed valvular orifice and can then be inserted well into the ventricle. This location is recognized by even more vigorous transmitted cardiac pulsations, and also by an increase in the systolic thrill transmitted to the operator's hand via the instrument (Figs. 24 and 25).

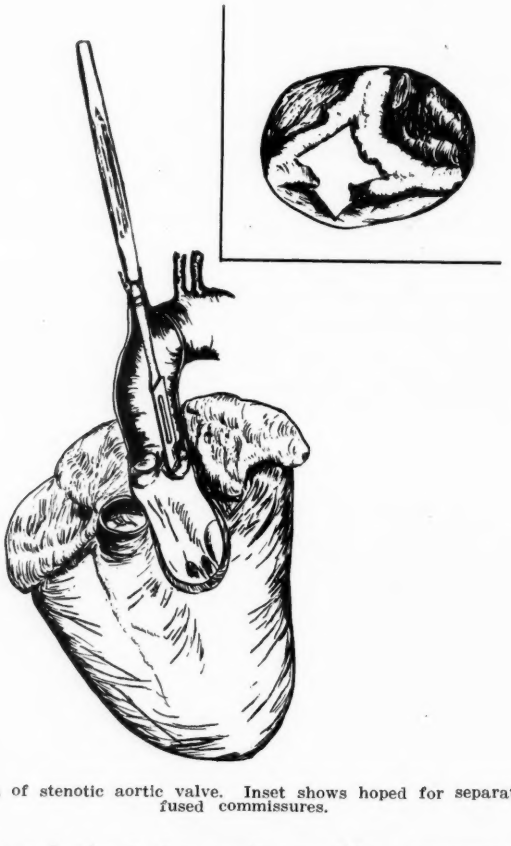


Fig. 25.—Dilatation of stenotic aortic valve. Inset shows hoped for separation of all three fused commissures.

The dilating mechanism is then gently opened by a turnscrew on the handle of the instrument, gradually dilating the narrowed orifice to or past the point of commissural separation. Blood flow through the aortic orifice is maintained by a lack of continuity of the dilating surface. After sufficient dilatation is deemed to have been accomplished the instrument is closed and removed. The carotid incision is repaired by a continuous suture of arterial silk.

We have performed this operation upon two persons with multivalvular lesions, one of which was severe aortic stenosis. The details of these operative

cases will be presented elsewhere. Both patients withstood the procedure well. Both presented postoperative objective evidence of enlargement of the aortic valve orifice, and both appeared clinically improved. Neither, by virtue of associated myocardial disease and of coexistent mitral regurgitation, was considered suitable for major thoracotomy and direct attack upon the heart. Both patients are recently postoperative and have not reached a point at which significant conclusions can be drawn regarding the permanence of the effects of valvular dilatation. It is even conceivable that repeated dilatations might be necessary after the elapse of time. There is no anatomical or surgical reason why repetition of the procedure should not be feasible.

SUMMARY AND CONCLUSIONS

1. Our entire experience with attempts to devise a reasonable surgical method for correcting or alleviating aortic stenosis has been presented.

2. Direct valve grafts and vein-valve grafts have been attempted without significant success.

3. Artificial valves have not been used, feeling that insertion of such valves beyond the orifices of the coronary arteries might well be unphysiological. When employed to replace the diseased aortic valve anatomically, such valves may be acceptable.

4. Attempts to by-pass the stenotic aortic valve by double aortic grafts incorporating intact aortic valves have been made. These grafts have anastomosed the aorta to the left ventricular chamber, both directly through the ventricular wall and via the left auricle and mitral route. For technical, physiological, and other reasons, these grafts may well be inapplicable in human aortic disease.

5. The procedures of Smithy and Parker have been duplicated. It is felt that the wide division of an aortic valve by either punch excision or simple incision produces regurgitation of greater magnitude than can be tolerated by diseased human hearts. The enormous hypertrophy of the left ventricle in aortic stenosis with its diminutive lumenal chamber effectively mitigates against prompt and adequate dilatation of this chamber, so essential for proper compensation in sudden, surgically produced aortic regurgitation.

6. A clinical attempt to divide a fused aortic valve into a bicuspid valve similar to the Brock procedure for congenital pulmonary valvular stenosis produced unexpected regurgitation and terminated fatally.

7. It seems probable that division of the fused valve commissures is desirable. This has not been accomplished as yet, either digitally or under direct cardioscopic vision.

8. Since the pathology of aortic stenosis lends itself more favorably to mechanical dilatation than does mitral stenosis, a method of dilatation has been developed. The relative ease with which dilatation can be accomplished retrogradely through the right carotid artery and ascending aorta has led us to abandon the more hazardous ventricular approach for the present.

9. Two patients with aortic stenosis have recently been submitted to mechanical dilatation using the cervical approach, with early clinical improvement.

ADDENDUM

Since submission of this manuscript for publication we have repeated the described technique in one case. Unfortunately a false passage was produced because of difficulty in entering the stenotic valve from above. This resulted fatally. Since then we have returned to the ventricular approach and have successfully dilated one stenotic aortic valve by that route.

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DISCUSSION

DR. A. E. BLOOMBERG, New York.—Dr. Bailey and his associates have presented an extremely interesting paper. As he pointed out, and recent writings of Dr. Blalock, Dr. Harkins, and others have attested, the full surgical attack upon the heart must await methods of visualizing within the heart. Such cardioscopes as have been made have relied on contact methods or utilized displacement chambers through which operation was not feasible. It occurred to me some time ago that a stream of fluid directed under great pressure against an object might displace the blood and might permit operation through such displaced blood. To that end we had several instruments made, and I shall discuss the latest one.

(Slide.) This shows the assembled cardioscope; the scissors at the end of the instrument is actuated by a rod at the end of the instrument; this makes for great cutting strength.

(Slide.) The fluid enters at this inlet and runs down a channel around the telescope. The next slide shows the instrument in cross section.

(Slide.) We have been able to visualize all the cardiac chambers and all the valves of the heart, approaching them through the auricles, the ventricles and, in the case of the aortic valve, the innominate artery. The valves move so rapidly that only a momentary view is afforded. However, when the approach is through the ventricle we have been able to pick up a papillary muscle or corda tendinea on the end of the scissors or hook, using another instrument we have, and follow it up to the valve, fixing the valve for a slightly longer period of time. In an attempt to fix the valve and simulate stenosis to some extent, we have opened the right auricle and sutured the tricuspid cusps together. Following closure of the auricular incision we have inserted the instrument through the right auricular appendage; it is then much simpler to visualize the valve and we have been able to cut the valve in several instances, although this instrument also has a defect in that the best focal point falls between the end of the telescope and the cutting scissors, but we feel we will be able to change that without too much difficulty.

It takes approximately two and one-half minutes for 500 c.c. of fluid to run through the cardioscope at 100 millimeters of pressure of mercury, but by utilizing short bursts of fluid and by removing blood from the femoral artery we have been able to obtain survivals. Some of our dogs have been operated upon two and three times. The dog seems to stand dislocation of the heart incidentally to the use of a straight instrument well, but this would not be true of human beings. Instruments that have an appropriate curve will be designed.

DR. FRANK S. DOLLEY, Los Angeles.—It is not possible by any statement of mine to detract in the least from the epochal work Dr. Bailey has done in connection with the surgical treatment of the aortic valve. I have no hesitation, therefore, in speaking of a tentative experiment of mine begun a number of years ago. It is of definite interest in connection with this work of Dr. Bailey's.

In 1925, following Graham's and Allen's experiments with their cardioscope, and shortly after Cutler's work on aortic valve division, I had constructed for me by an instrument maker in London a steel fingernail. It was so made as to permit the distal phalanx of my right forefinger to slip snugly into this sleevelike instrument. There was an opening to admit my own fingernail. My this means, control of the steel fingernail could be carefully maintained. Another large palmar aperture left exposed the pad of the distal phalanx, so that orientation could be established and maintained.

The purpose of this steel fingernail was by its use to convert a mitral stenosis to a regurgitation. It was planned to introduce the index finger into the left atrium through the auricular appendage. The exposed pad of my own finger would reach the stenotic valve. By means of the hard steel fingernail immediately distal to my own, with a scissorlike cutting motion it would be possible to divide a valve leaf sufficiently to produce conversion from stenosis to regurgitation. At the proximal rim of the steel sleeve there was a small hole. A strong thread carried through this hole and out to the other hand would prevent the loss of the instrument as the index finger was being withdrawn.

I regret very much that for several reasons I have not yet attempted by this means to convert a mitral stenosis to a livable regurgitation.

THE EXPERIMENTAL CREATION AND CLOSURE OF AURICULAR SEPTAL DEFECTS

HENRY SWAN, M.D., GEORGE MARESH, M.D. (BY INVITATION), MARVIN E. JOHNSON, M.D. (BY INVITATION), AND (BY INVITATION) GEORGE WARNER, M.D.
DENVER, COLO.

INASMUCH as the clinical auricular septal defect is a static structural lesion, it would appear to be a type of disease which should be amenable to surgical repair. The malformation is apparently fairly common,[1, 2] and because of gradually progressive changes in hemodynamics, the life span of these patients is usually curtailed. Clinical attempt at closure of this defect has been reported.[3] Lack of data on oxygen saturations in the right auricle before and after the attempted closure, however, make analysis of the effectiveness of the procedure impossible. This paper is a report of our experience with the creation and closure of auricular septal defects in the experimental animal.

THE CREATION OF THE DEFECT

For the purpose of studying methods of closure, it is desirable to create an experimental defect which lies as nearly as possible in the anatomic location of the common clinical lesion. Congenital septal defects occur in two separate areas having different embryologic origins as clearly described by Patten.[4] In the first type, which occurs uncommonly, the defects are due to arrested development of the septum primum and lie in the extreme inferior portion of the septum directly overlying the atrioventricular valves. In the second and by far the more common type, the defects result from arrest in the descent of the septum secundum coupled with abnormally extensive resorption of septum primum. This produces essentially a failure in the development of the superior margin of the foramen ovale and these defects thus extend from approximately mid-septum into the upper anterior quadrant. It is with the experimental creation of this second lesion that we are primarily concerned.

Our initial attempts to create a defect were made by inserting a narrow knife blade through the auricular wall and placing an elliptical incision blindly through the septum. We found it was quite possible to make the cut 1 or 2 cm. in length, but these incisions invariably healed rapidly, and three weeks later, inspection of the septa revealed them to have returned to an intact and essentially normal state. Recently, Martin and Essex[5] have reported better success and an occasional lasting defect using this method.

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However, we concluded that it would be necessary to actually remove a segment of the septum if success were to be obtained. The initial approach was by means of a rotary punch applied blindly through the wall of the auricle using a purse-string suture. Because the septum is so flexible and because it is in constant motion, our success with this method was minimal. In one animal we managed to create a ragged defect about 1 cm. in diameter, which had begun to heal over when inspected at two weeks.

A rotating blade around the end of a cardioscope encountered the same difficulties. Although it was possible to identify visually the various landmarks in the auricle and on the septum, and thus the effort was directed more accurately at the proper anatomic area, the results were equally disappointing.

It appeared desirable, therefore, to attempt to create the lesion under direct vision. Early in 1948, we devised an instrument out of a standard type sponge forceps with which it was possible to approach the septum with a limited but bloodless field. By bending the blades of the forceps to form a circle one could compress the two walls of the auricle against the septum over an area of 1.5 cm. without embarrassing the action of the heart for periods of from four to as long as thirty minutes. Incision in the right auricular wall brought us directly down to the septum and a defect about 1 cm. in diameter, roughly circular in shape, could be made with the scissors or a small sharp knife. The animals tolerated this procedure well on the whole, but to our disappointment, we found that defects of this size, in spite of the fact that there had been loss of substance, uniformly tended to heal over spontaneously in a period of four to eight weeks. For this reason, we abandoned this method.

At about the same time Doderill[6] in Detroit was developing quite independently a similar instrument. In his subsequent report, the illustrated defects, which originally were even larger than ours, appeared to be healing at one month and looked no bigger than the coronary sinus.

At about this time, August of 1948, Blalock and Hanlon[7] published their ingenious method for the creation of a communication between the auricles. This shunt, however, is placed well posterior and superior on the wall of the right auricle and thus lies behind and above the usual anatomic site of the clinical defect. For our purposes, therefore, this procedure did not appear ideal; but if one desires to establish a permanent auricular shunt for experimental or therapeutic reasons, we believe this is the method of choice.

Accordingly, we turned to an attempt to excise the septum under direct vision with the auricle open and the blood flow temporarily occluded. This is a technique which was used by Templeton and Gibbon[8] in their experiments on the tricuspid valve.

The chest is opened by an intercostal incision in the fourth interspace on the right side. The azygos vein is divided between ligatures near its entrance into the superior vena cava. The superior and inferior venae cavae are onw mobilized and umbilical tapes are passed beneath them to serve as temporary ligatures. The pericardium is opened widely in a vertical direction anterior to the right phrenic nerve, and retracted by silk sutures. Two sutures are placed in the auricular wall to demarcate the ends of the proposed incision which is about 3 cm. in length, running vertically, with the lower end at

the point of junction of the inferior vena cava with the auricle and about 1 cm. anterior to the attachment of the pericardium. Two additional retraction sutures are placed about 2 mm. apart, straddling the midpoint of the proposed incision. One assistant now pulls up on the hemostatic umbilical tapes occluding the venae cavae. This is his only responsibility, and he maintains this control throughout the procedure until instructed to release by the operator. The two medial silk retention sutures are held by the first assistant. The operator makes the auricular incision with the scissors and then immediately sucks out the auricle with the sucker. There is a very small amount of blood entering the auricle from the coronary sinus. The landmarks are identified, particularly the coronary sinus. A point in the septum 1 cm. superior and 1 cm. posterior to the coronary sinus is grasped with the sharp arterial forceps, elevated, and excised with the scissors. A roughly circular piece of tissue about 2 cm. in diameter is removed. Surprisingly little blood emerges from the left auricle through this defect. It will be remembered that blood flow through the lesser circuit has been halted during the procedure and since the left auricle is dependent, the force acting to expel blood upward through the septal hole is minimal (Fig. 1).

Fig. 1.—Operative view of freshly created auricular septal defect. The venae cavae are temporarily occluded and the wall of the right auricle is open. The defect is superior and posterior to coronary sinus.

The chest cavity is now immediately flooded with saline solution. The operator pulls upward on all four auricular retention sutures controlling the extremities of the incision and the first assistant applies the curved spring clamp. The upward pull on the umbilical tapes is now released, and blood flow from the venae cavae, which has been obstructed between one and two minutes, is at once resumed. The incision in the auricle is now closed at leisure with everting mattress sutures of 000 silk which effects an endocardium-to-endocardium closure. The spring clamp is removed, the pericardium closed, and the chest wound repaired. The animal's recovery is uneventful.

It is remarkable that the disturbance in cardiac rhythm is so slight. In no instance did either auricular or ventricular fibrillation supervene. Neither did any evidence of interference with the sinoauricular pacemaker occur. One pitfall of the operation is the possibility of exceeding the margins of the septum and cutting through the wall of the right auricle. Very accurate placement of the septal excision is essential.

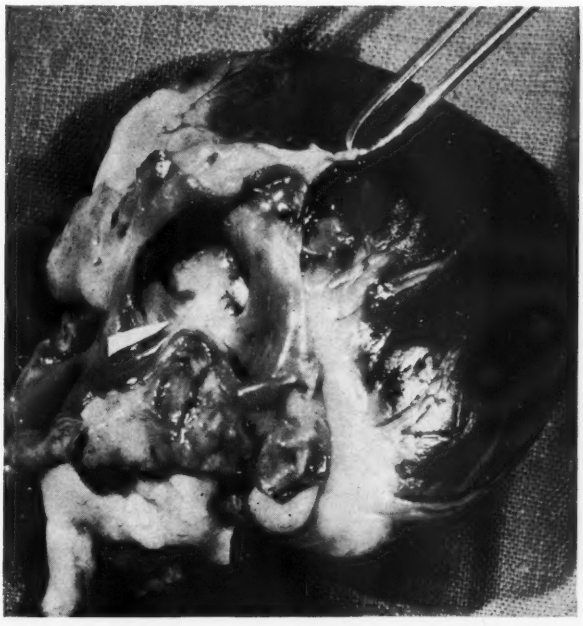

Fig. 2.—View through right auricle of healed septal defect three months after creation. Arrow points to scar in septum; small pledget is in coronary sinus.

We have observed two complications. In one animal death occurred two hours postoperatively. Autopsy revealed air emboli of the left coronary arteries. This is the only animal which had any symptoms of air embolus. In the experience of Martin and Essex with this technique, air embolism was common. It is possible that our method of immediately flooding the chest cavity with saline after the defect was cut was helpful in preventing this complication. In another, upon second operation for the purpose of repairing the defect, a firm intraluminal thrombosis was found in the right auricle adherent to the incision in the auricular wall.

The fate of septal defects created in this fashion is most extraordinary. In spite of the removal of the major portion of the septum, healing commonly occurs in a period of from two to three months, often with complete restoration of a functional septum. It would appear that the auricular septum has great powers to repair a traumatic defect, that careful endocardium-to-endocardium

coaptation is essential if the defect is to persist (as in the Blalock-Hanlon procedure), and that blind or open surgical incisions or excisions of septum will not consistently remain patent (Fig. 2).

However, for the purposes of experimental closure a preparation was accomplished which simulated the clinical lesion, if closure was attempted within a month of the creation of the defect.

CLOSURE OF THE DEFECT

In 1947, Cohn[9] described an experimental method for the closure of small auricular septal defects in the dog. The lateral wall of the right auricle was pushed against the septum and two sutures were placed to hold it in this position. A wire snare was threaded into the auricle around this portion of wall, and the button-shaped section attached to the septum was cut free, allowing the rest of the wall to revert to normal position. The hole in the auricle left by this maneuver was sutured closed.

This ingenious operation seemed to us to have two potential dangers. During the period of initial invagination of the wall, blood flow from the venae cavae was disturbed and cardiac irregularities were commonly encountered. Second, after excision of the segment of wall, the surface exposed to the internal blood flow in the right auricle was the external surface of the myocardium; it was not lined with a smooth endocardial layer. It seems likely that the factors most suitable for the initiation of intra-auricular thrombosis were thus established. If a method utilizing auricle wall could be devised which did not interfere even temporarily with blood flow and which left exposed to the blood stream only endothelialized surfaces these potential dangers might be eliminated. Such a method is here presented.

The fundamental concept of this technique is to invaginate both auricular appendages and to fasten their tips firmly together through the septal defect. This converts the lumen of the auricle to a hollow space eccentrically "doughnut" in shape, entirely lined with endothelium. No interference with blood flow is encountered. The procedure is as follows:

Under intravenous nembutal anesthesia, using intermittent positive pressure endotracheal oxygen, the animal is placed supine on the operating table and both sides of the chest are prepared and draped. Bilateral anterior intercostal thoracotomies are placed in the fourth interspace, and rib retractors inserted. Eight cubic centimeters of 2 per cent procaine are injected into the pericardium. Attention is first directed to the left side. A T-shaped incision is made in the pericardium over the tip of the left auricle lateral and posterior to the emergence of pulmonary artery. Left auricular tip is identified. A moist drape is now placed over the wound and activity is shifted to the right side. A vertical incision is made in the pericardium the length of the auricle, just anterior to the phrenic nerve. The right auricular tip is seized with the toothed forceps and a purse-string suture of 000 silk is placed at the very apex. The eye end of a standard surgical probe is thrust through the loop into the auricle and the purse string is tightened to effect hemostasis. The bent probe is advanced by feel into the inferior vena cava. It is then drawn slowly upward feeling with the tip along the septum seeking the defect. The coronary sinus may be entered, in which case the probe can be felt in the atrioventricular groove posteriorly. From here the defect lies superior and posterior. If the tricuspid valve is entered, the probe is too far anterior. Usually only one or two tries are sufficient to pass

the probe through the defect into the left auricle. Care must be taken that it does not progress out one of the left pulmonary veins. The left incision is now inspected and by feel and direct vision the tip of the probe is manipulated until it lies in the very apex of the left appendage. It is pushed through the muscle at that point (Fig. 3).

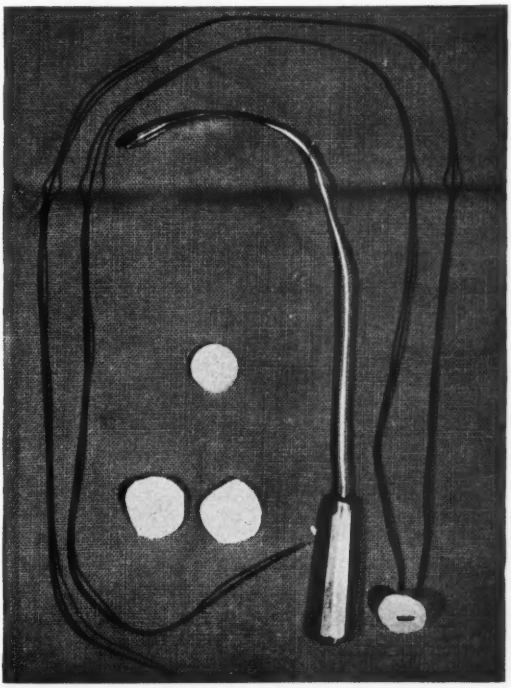

Fig. 3.—A bent surgical probe, two polyethylene buttons, and two pieces of Gelfoam are the only special equipment needed for inversion of the auricular appendages.

The first assistant now rapidly threads the eye of the probe with the two ends of a strand of No. 1 silk on which has previously been threaded a circular button of stiff Polythene, 1½ to 2 cm. in diameter. A piece of Gelfoam lines the inner side of the button. The probe is now entirely withdrawn carrying with it the silk strand. This is pulled up to snug the Gelfoam against the left tip and to start the inversion of the left appendage. A similar piece of Gelfoam and Polythene button is now threaded onto the ends of the silk, the first throw of a surgeon's knot is placed, and the throw gradually but firmly tightened until it is quite snug. This maneuver inexorably draws the inverted tips of the auricles toward each other until they abut through the septal defect. The two buttons can be identified by feel as having been brought into close apposition in the midline. The knot is finished and the ends cut.

This entire maneuver can be accomplished with almost no loss of blood, and has not been accompanied by any severe disturbance in cardiac rhythm. The heart does not need to be displaced, and no interference with blood flow is encountered at any time. It remains only to repair the pericardium, expand the lungs, and close the incisions in the usual fashion.

A series of ten dogs with artificially created defects have been closed using this technique. The condensed operative protocols of these animals are seen in Table I.

TABLE I. CONDENSED PROTOCOLS OF CLOSURE OF AURICULAR SEPTAL DEFECT

DOG NUMBER	DATE DEFECT CREATED (1949)	DATE DEFECT CLOSED (1949)	REMARKS
125	March 15	April 8	Killed Jan. 18, 1950. A 2 cm. defect approximately one-half closed by repair. Remainder of defect closed by small organized thrombus
141	April 15	May 11	Sacrificed Sept. 27. An 8 mm. defect was approximately two-thirds closed by repair
145	April 22	May 9	Dog still alive and healthy. Normal ECG, and normal cardiac catheterization
147	April 25	May 25	Sacrificed Dec. 20. A 1 cm. defect was two-thirds closed by repair
148	April 27	May 31	Died 8 hrs. postrepair of bilateral atelectasis. A 6 mm. defect was totally closed by repair
149	May 2	June 1	At second operation, a firm clot felt in right atrium. Dog died June 10, of empyema. The 8 mm. defect was totally closed. An organized thrombosis was found in right atrium
161	June 6	June 28	Sacrificed Dec. 20. A 1 cm. defect was completely closed by repair. Heart appeared normal in size
164	June 8	June 30	Dog still alive and healthy
185	July 8	July 27	Sacrificed Sept. 24. The 9 mm. defect was completely closed by repair
211	Aug. 3	Aug. 25	Dog died on table during skin closure. Cause of death not identified. A 6 mm. defect was well closed by the repair

DISCUSSION

The effect on the cardiovascular hemodynamics of the creation of these septal defects is usually quite minimal within the period of time which they have been observed. The dogs remain quite active and apparently healthy. Occasionally, at second operation the right auricle appears moderately enlarged. The left auricle appears normal.

Cardiac catheterization studies were performed on the animals to evaluate changes in hemodynamics occurring after creation of the defect and after the subsequent repair. An increase of 1.0 volume per cent or more in the oxygen content between the superior vena cava and the right ventricle was chosen as the minimal criteria necessary to suggest flow of oxygenated blood through the septal defect. Table II is a summary of the catheterization studies. It will be seen that in most instances, the status of the auricular septum was accurately reflected by the oxygen saturation studies; but in four animals (Group 3) the

TABLE II. CARDIAC CATHETERIZATION STUDIES

A. Creation of Defect		
1. Abnormal blood flow; defect proved	No. 125, 145, 147, 148, 161	Catheter revealed status
2. No abnormal blood flow; no defect present	No. 141, 159, 163	Catheter revealed status
3. No abnormal blood flow; defect proved	No. 117, 149, 185, 211	Catheter failed to reveal status
B. Repair of Defect		
4. Returned to normal blood flow	No. 125, 145, 147, 161	
5. Did not return to normal flow	None	

catheterization failed to reveal a defect which was subsequently proved to exist. Apparently, at the time of the study, there was no significant left-to-right flow of blood through the defect. It is probable that in the early stage of this abnormality, blood flow may be variable.

What is the functional efficiency of the method of closure? In the four animals which had evidence of abnormal blood flow before repair, catheter studies following repair revealed a return to normal hemodynamics. This data is presented in Table III. We think the evidence is suggestive that abnormal blood flow through the experimental defect is effectively prevented by the operation.

Fig. 4.—Seen from above, the inverted auricular tips abut through the septal defect. Autopsy specimen obtained from Dog No. 161, six months following repair, shows smooth endothelial surfaces, lack of thrombosis, and effective closure of defect.

The bilateral thoracotomy was well tolerated by the animals. In only one (No. 148) was atelectasis a significant complication, and it is probable that we were careless in re-expanding the lungs in this animal at the close of the operation.

Intra-auricular thrombosis occurred in only one instance, and this was apparently a result of the creation of the defect rather than of the repair, since it was felt to be present at the second operation. Thrombosis, however, might well occur if auricular rhythm were disordered. This complication did not occur in any of the animals in this series. It is possible that the enlarged, dis-

TABLE III. EFFECT OF CLOSURE OF SEPTAL DEFECT ON CATHETERIZATION FINDINGS (GROUP 4, TABLE I)

DOG NUMBER	VOL. PER CENT O_2 SATURATION (BEFORE CLOSURE)				VOL. PER CENT O_2 SATURATION (AFTER CLOSURE)				O_2 SAT. DIFF. S.V.C. TO R.V.	
	SUPERIOR VENA CAVA	RIGHT AURICLE (1)	RIGHT AURICLE (2)	RIGHT VENTRICLE	SUPERIOR VENA CAVA	RIGHT AURICLE (1)	RIGHT AURICLE (2)	RIGHT VENTRICLE	BEFORE	AFTER
125	8.5	8.1	9.1	11.0	10.5	10.5	10.3	11.0	1.5	.5
145	7.3	8.0	7.3	8.9	10.3	9.8	10.8	9.7	1.6	- .6
147	9.5	11.2	10.9	11.2	9.3	8.0	8.3	9.3	1.7	0
161	7.1	7.0	8.0	8.8	12.0	11.6	12.2	12.2	1.7	.2

tended auricles of the clinical patient would not react so kindly to this manipulation as did the auricles of these essentially normal dogs.

There was no evidence of any interference with blood flow or with auricular function by the inverted auricular tips. This is apparently because anatomically the inversion occurs in the upper anterior quadrant of the lumen of the auricle, while the blood flow occurs primarily in the posterior and inferior quadrants. In addition, the intraluminal auricular pressure apparently compresses the inverted appendage so that its diameter, as it traverses the auricle, is usually quite small, much less than the size of the button at its tip (Fig. 4).

In some of the specimens, the edge of the defect had healed firmly to the auricular appendage passing through it either totally or in part. It is possible that this is related to the traumatic origin of the defect and would not occur in defects which were congenital.

SUMMARY

1. A method for the creation under direct vision of an auricular septal defect in dogs, which simulates anatomically the congenital clinical defect, is described.

2. These defects have a strong tendency to spontaneous closure by healing.

3. An operation for the anatomical and functional obliteration of these experimental defects by inversion of the auricular appendages has been devised which is well tolerated by the animals.

4. The effectiveness of this procedure in reverting abnormal blood flow to normal is suggested by cardiac catheterization studies.

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DISCUSSION

DR. F. D. DODRILL, Detroit.—I rise to comment on a few points about atrial septal defects with which we have had some experimental and clinical observation. Some of you will recall that last year I showed a method by which we could excise the major portion of the atrial septum under direct vision and at the same time close it by a method of suture. We have tried leaving these atrial defects open and found, as Dr. Swan did, that they nearly all close in a matter of a few months. Moreover, it has been our experience that we could not simulate the hemodynamics of the disease in the human being. That, of course, is primarily the reason why the defects close in the experimental animal, because the blood flow is not sufficiently great to maintain its patency. It would be nice if all atrial defects in the human being were in a position in the center of the septum. It is difficult, indeed, to get an accurate idea as to where the majority of them are, from the pathologic literature. There are directly contradictory reports; some will say they are in the so-called center of the septum, and others report that the majority are in the inferior portion of the septum which does not correspond to the hole which we create in the center. It has been our experience in the few cases that we have explored, that the atrial defect has been directly in continuity with the bicuspid and the mitral valves. It is therefore a sort of half-moon defect, the lower and inferior portion of the circle being the valves themselves.

It would seem to me that the type of defect would not be so amenable to the type of closure which Dr. Swan has shown, because of the interference with ventricular filling.

DR. SANFORD E. LEEDS, San Francisco.—I would like to discuss one point regarding the persistence of artificial septal defects. As you know, there are several methods of producing septal defects, and I think the method we use is inferior to the visual methods Dr. Swan and Dr. Dodrill have mentioned today. We use a modified nasal septal punch of the Yankauer type, and the main advantages are that the method is extremely simple and there is no trauma to the right auricle. We had one animal in which the defect had persisted for 162 days at the time it was sacrificed, and apparently the defect was not closing any further at that time. Why this one persisted I do not know.

(Slides.) The modification of the septum punch consists of a perforated sheet of metal which is soldered over the punch in order to retain the removed portion of the interauricular septum. The left auricular appendage is opened and the septum punch is inserted. The left forefinger is used to palpate the location of the septum between the superior and inferior cavae. It is possible to locate the exact position where the opening is to be made, and then a bite is taken, pressing down on the left forefinger with the punch. It might appear that one would go through both layers and open the outer wall of the right auricle, but this did not occur.

(Slide.) This colored photograph shows the left side of the heart opened with the persistent septal defect which stayed open five and one-half months. Here you see the right side of the septum with the persistent opening which measured 1.4 cm. in diameter.

DR. SWAN (closing).—I would like to thank Dr. Dodrill and Dr. Leeds for their comments. The septal defect which occurs just above the valves, also embryologically carefully described by Patton, is the result of failure of complete descent of the septum primum, and is a very definite clinical entity as Dr. Dodrill stated. The incidence of the various types has not been well worked out. I would agree entirely that it may be impossible in clinical patients to predict preoperatively which type of lesion is present.

A PHYSIOLOGIC EVALUATION OF VAGUS SECTION FOR BRONCHIAL ASTHMA

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BRONCHIAL asthma has been considered an expression of tissue hypersensitiveness. Certain instances, however, are regarded as something more than resulting entirely from a single process such as allergy, infection, psychoneurosis, or irritation of the mucous membranes of the upper respiratory tract. Various surgical procedures have been postulated, planned, and accomplished on the extrinsic pulmonary nerves in attempts to relieve "intractable" bronchial asthma. Of these, unilateral cervical sympathectomy, stellate ganglionectomy, bilateral cervical sympathectomy, unilateral cervicodorsal sympathectomy, and bilateral resection of the posterior pulmonary plexus have gained some application. The results, in general, are still debatable, yet in certain instances brilliant success has been reported. This has stimulated continued effort toward a surgical approach.

We have reported our studies on the neurophysiology of the tracheobronchial tree. In these a review of the literature pertinent to the anatomy of the extrinsic pulmonary nerves was presented.[1-4] In brief, the bronchi receive a dual nerve supply, derived from the upper thoracic sympathetic and vagus nerves. These nerves meet at the level of the pulmonary hilus to form the anterior and posterior pulmonary plexus, where they are stated to intermingle freely with a partial crossing of some of the fibers to the opposite lung. The sympathetic efferent fibers, whose cell bodies are located in the first four thoracic spinal ganglia, communicate with the sympathetic chain through the upper three white rami communicantes. The sympathetic efferent fibers arise from nerve cells in the intermediolateral cell column of the spinal cord and traverse the upper four thoracic white communicating rami to reach the sympathetic chain. There is evidence that a majority of these fibers pass to the stellate ganglion, where a synapse is made with the postganglionic fibers to the lung. The vagal afferent fibers, whose cells of origin are bipolar and located in the nodose ganglia, are distributed peripherally to the tracheobronchial tree, and centrally to the nucleus of the tractus solitarius. The vagal efferent fibers arise from cells in the dorsal motor nucleus of the vagus and are distributed peripherally to the tracheobronchial tree where they synapse with dendrites of nerve cells from which originate the postganglionic fibers.

Physiologic studies have demonstrated that vagus stimulation and parasympathomimetic drugs cause bronchoconstriction, whereas sympathetic stimu-

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lation and sympathomimetic drugs produce bronchodilatation. In this regard, the work of Dixon and Brodie,[5] and Dixon and Ranson[6] is of importance, inasmuch as they established a physiologic basis for the attempted relief of asthmatics by surgical means. By measuring the fluctuating volume of the right middle lobe of a cat's lung they demonstrated that vagal stimulation consistently produced bronchoconstriction, whereas stimulation of the upper three thoracic sympathetic ganglia or the stellate ganglion resulted in bronchodilatation. The existence of bronchodilator fibers in the vagus nerve and the presence of bronchoconstrictor fibers in the sympathetics was occasionally observed; however, this was considered unusual and insignificant. Partial crossing of sympathetic and vagal fibers to the opposite lung was usually demonstrable. In addition they observed that stimulation of the central end of the cut vagus nerve, after both vagus trunks had been sectioned, produced reflex bronchodilatation. By repeated transections of the nerve tracts, they concluded that the reflex pathway traversed the vagal afferent fibers to the medulla, passed from the medulla to the lateral columns of the cervical cord, and then was carried through the first, second, and third thoracic white communicating rami to the sympathetic chain, to the stellate ganglion, and on through the "accelerator nerve" to the bronchi. Likewise, they noted that reflex bronchoconstriction could be readily obtained by stimulating the central end of various afferent nerves such as the sciatic, crural, trigeminal, glossopharyngeal, and vagus, but in no instance was reflex bronchoconstriction found after bilateral section of the vagus trunks. The probability of a higher distribution of these nervous pathways was suggested by the bronchoscopic observations that the presence of bronchoconstriction or bronchodilatation is determined in part by emotional factors. Faulkner[7] observed that thoughts of insecurity and frustration resulted in bronchoconstriction, whereas thoughts of a pleasant and desirable nature produced bronchodilatation.

That the bronchi normally constrict during the expiratory phase and dilate during the inspiratory phase of respiration is a well-known phenomenon. In this regard Ellis has satisfactorily demonstrated that the rhythmic movements of the bronchi are passive and entirely due to the movements of the thoracic wall.[8] We are in agreement with this conclusion in that we have been unable to observe any bronchial movements during thoracotomy, that is, after the negative pleural pressure has been released.

In 1930, Kountz and Koenig[9] reported that vagal stimulation apparently increased the secretion per unit area of bronchial mucosa in the dog, whereas stimulation of the cervical sympathetics caused little change, or possibly a slight decrease in the amount of secretion. Subsequently, Florey and associates[10] demonstrated that stimulation of the peripheral end of the cut vagus and inferior laryngeal nerves in the cat increased the amount of tracheal secretion. The effect was abolished by the administration of atropine. Stimulation of the central ends of the vagus nerve caused the tracheal glands to secrete reflexly when one of the vagus nerves remained intact. In addition, we have observed during bronchoscopy that the administration of parasympathomimetic drugs

results in bronchorrhea. That sympathetic stimulation may cause vasoconstriction of bronchial vessels is suggested by the bronchoscopic observation of the blanching of bronchial mucosa by the subcutaneous or topical application of adrenalin.

On the basis of these studies and the findings of many other observers, Alexander[11] presented the following table pertaining to the neurophysiology of the bronchial tree:

Bronchial	*Sympathetic stimulation*	*Vagal stimulation*
Muscles	Relaxation	Contraction
Glands	Inhibition	Secretion
Vessels	Constriction	Dilatation

In order to apply the known neurophysiology of the bronchi correctly in the surgical treatment of intractable bronchial asthma, it is necessary to consider the pathologic physiology of this condition. Most investigators believe that the characteristic wheezing, dyspnea, and prolonged expiration of asthma are due to a narrowing of the bronchial lumen. Inasmuch as the larger bronchi are supported by cartilaginous rings, it is reasonable to assume that relatively the greatest obstruction occurs in the smaller bronchi. Although the exact mechanism responsible for the decreased bronchial caliber has been the subject of considerable debate, two leading theories have received wide acceptance: (1) spasm of the bronchial muscle, and (2) edema of the bronchial walls with excessive secretion of mucus. There is considerable evidence to substantiate each theory; however, Alexander[12] stated: "It is probable that since vagus stimulation, which is the nerve impulse that initiates an attack, causes all three lesions, no one, but all, play a role. In the earlier stages of the disease, edema and bronchial constriction are probably the most important factors, since the mucous glands are small and the production of mucus scant. In long standing asthma increased, thick, tenacious mucus is probably the most important factor in bronchial obstruction."

Unfortunately pathologic confirmation is limited in that relatively few asthmatics die of the disease, and it is difficult to apply the findings of microscopic sections to a functional disturbance. The lack of uniformity of the findings of the few post-mortem examinations on asthmatics is probably due to the variable duration of the disease, the fact that some patients died during a paroxysm while others died of intercurrent disease and the presence of complications, such as pneumonia, heart disease, and emphysema. However, sufficient correlating data are available to permit of certain general statements. Grossly the lungs are usually emphysematous, associated with small intervening areas of atelectasis; the bronchi contain a thick, tenacious sputum which may partially obstruct the lumina; the bronchial walls are thickened, and the bronchial mucosa is usually hyperemic and thrown into folds. In patients dying during a paroxysm constriction of the medium-sized bronchi of 5 mm. in diameter has been reported, whereas the more distal bronchi and the alveolar sacs are distended with trapped air. This gives rise to the belief that the primary pathologic physiology of the asthmatic occurs in bronchi of approximately 5 mm. in diameter.

The microscopic pathology of these bronchi includes:

1. Metamorphosis of the normal ciliated cells to goblet cells and, later, metaplasia to pseudostratified squamous epithelium.
2. Excessive mucus within the bronchial lumen.
3. Infolding of the bronchial mucosa which partially obstructs the lumina.
4. Widening of the submucosal layer in some instances to twice its normal size, which is thought to be due to hyperemia and round cell infiltration, especially eosinophils.
5. Hypertrophy of the bronchial smooth musculature.

On the basis of experimental work demonstrating the nervous control of the bronchial tree, many investigators have suggested that an increased number of bronchomotor impulses cause the bronchospasm, excessive bronchial secretion, and edema responsible for the asthmatic paroxysm. According to this hypothesis, interruption of the proper nerve pathways should alleviate the symptomatology of bronchial asthma. Kümmel[13] was the first to report such an operative procedure in 1923. Although he realized the vagus nerve was the main bronchomotor nerve, he excised the superior, middle, and inferior cervical sympathetic ganglia along with a portion of the stellate ganglion on one side. He reported good results in three cases. Subsequently a number of patients in European clinics were subjected to various operative procedures directed toward the unilateral or bilateral excision of the cervical sympathetic chain and the stellate ganglion. In 1924, Kappis[14] transected the right vagus trunk below the recurrent laryngeal nerve with good results. This led to a combined operative procedure in which unilateral vagotomy and unilateral cervical sympathectomy were performed. Later Kümmel[15] advocated section of the posterior pulmonary rami inasmuch as Bräucher[16] had demonstrated that both sympathetic and vagus fibers supplied the posterior pulmonary plexus and only at this point could complete denervation of a lung be accomplished.

Phillips and Scott[17] in 1929, reviewed over 300 cases collected from the literature of patients with asthma who had received surgical treatment. Unfortunately, many cases had been reported before sufficient time had elapsed postoperatively to allow of critical evaluation. Of those considered eligible for analysis 30 per cent were believed to be "cured," 18 per cent improved, and 45 per cent were unimproved. In 1938, Rienhoff and Gay[18] reported on 16 patients in whom bilateral resection of the posterior pulmonary plexus had been performed. In 1942, further observations were submitted by these investigators[19] in 21 patients, 8 of whom received 50 to 100 per cent relief, and 13 of whom were considered failures.

More recently Miscall and Rovenstine[20] have reported on the value of Novocain block of the stellate and upper four thoracic sympathetic ganglia as a diagnostic procedure in determining the role the sympathetics play in asthma. In all patients successfully blocked, immediate improvement was noted in 78 per cent. The patients responding to Novocain block were considered to be the candidates most likely to receive permanent relief from excision of the right stellate and upper thoracic ganglia. In 21 patients subjected to unilateral

cervicodorsal sympathectomy complete relief of asthma was obtained as long as two years subsequent to surgery at the time of the report.

It thus becomes evident that surgical procedures directed toward either the vagus or sympathetic nerves have been reported as yielding good results. Although the rationale for vagotomy is more clear it is difficult to comprehend how sympathectomy could be equally successful, inasmuch as the vagus is considered to be the "bronchomotor nerve." Theoretically, if sympathetic-parasympathetic antagonism exists, sectioning of the sympathetic supply to the bronchial tree should result in unopposed bronchospasm, thus producing an exacerbation of the asthmatic state. That such may occur is demonstrated by the work of Miscall and Rovenstine, in which they caution that Novocain block of the cervicodorsal sympathetics may precipitate status asthmaticus.

In an attempt to explain the good results following unilateral and bilateral cervical sympathectomy investigators have offered the following theories:

1. Bronchial asthma in some instances is due to a reflex mechanism initiated by irritation of the tracheobronchial tree. This gives rise to nerve impulses which traverse sympathetic afferent fibers to the medulla where connection is made with vagal efferent bronchoconstricting fibers. Hence, sympathectomy interrupts the reflex arc on the afferent side.

2. The sympathetic nerves to the tracheobronchial tree contain some bronchoconstricting fibers, as demonstrated by the work of Dixon and Ranson,[6] Binger and associates,[21] and Hebb.[22] Sympathectomy theoretically diminishes the number of bronchomotor impulses, thus decreasing the degree of bronchospasm, secretion, and edema.

3. Co Tui and associates[23] demonstrated that the bronchi were more sensitive to adrenalin following cervicodorsal sympathectomy. Theoretically the small amount of circulating adrenalin in sympathectomized patients may be sufficient to inhibit bronchospasm, thus diverting the asthmatic paroxysm.

Little basis for the first theory is afforded by the findings of our previous studies.[2, 3] Two afferent functions of the bronchial tree were shown to be carried in the majority of patients by the homolateral vagus nerve. In brief this was demonstrated by the bronchoscopic observation that electric stimulation of the nonanesthetized tracheobronchial mucosa resulted not only in paroxysmal cough, but also in pain referred to the anterior chest wall or cervical region. These studies were repeated in patients in whom unilateral vagotomy had been performed below the origin of the recurrent laryngeal nerve. (This latter procedure was performed in an attempt at palliation of patients found to have inoperable bronchiogenic carcinoma at the time of exploratory thoracotomy.) In contrast to the previous observation, electric stimulation of the homolateral nonanesthetized main bronchus failed to elicit cough or pain in all but three patients. These results not only suggest that the afferent fibers which transmit pain from the bronchial tree but also the afferent fibers transmitting bronchial impulses resulting in initiation of the cough reflex are carried by the homolateral vagus nerve. The findings in the three patients found to have pain of homolateral bronchial origin following unilateral vagotomy suggest that the afferent nerve supply of the bronchial tree is derived in part from the contralateral

vagus nerve. In these investigations there was no physiologic evidence that the sympathetic system supplies afferent fibers to the bronchial mucosa. If bronchial asthma is due to a reflex mechanism initiated by irritation of the bronchial mucosa, and if interruption of the afferent side of the reflex arc is the desired effect, then from the preceding observations it would appear that vagotomy should be the procedure of choice.

Although there is evidence that bronchoconstricting fibers are carried in the sympathetic system, the preponderance of experimental data indicates that the vagus is the main bronchomotor nerve. Therefore, according to the second hypothesis, if the desired effect in the surgical treatment of asthma is to decrease the number of bronchomotor impulses, again vagotomy would seem to be the procedure of choice.

It is difficult to conceive how unilateral interruption of either the vagus or sympathetic system could be any more than partially successful in that the pathologic physiology of asthma is a bilateral phenomenon. In addition anatomic and physiologic investigations have demonstrated that each side of the bronchial tree receives nerve fibers from the contralateral vagus and sympathetic nerves. Therefore any unilateral procedure would not completely interrupt that particular nervous supply to the homolateral bronchial tree. In this regard the work of Rienhoff and Gay[18] is more logical in that complete denervation of the bronchial tree was performed by bilateral resection of the posterior pulmonary plexus. Although we are in agreement with the performance of a bilateral procedure, we believe that the sympathetic system should be left intact. If the theory of sympathetic-parasympathetic antagonism is correct it appears from the foregoing data and discussion that bilateral vagotomy, leaving the bronchodilating sympathetic fibers intact and unopposed, would be the logical operative procedure. From an anatomic and physiologic standpoint to achieve complete parasympathectomy of the bronchial tree, leaving the sympathetic nerves intact, the surgical procedure should consist of a bilateral transection of the vagus nerves above the origin of all branches of the pulmonary plexus.

In previous studies we have demonstrated that unilateral section of the vagus nerve immediately below the origin of the recurrent laryngeal nerve could be performed without any adverse sequelae. There appeared to be no contraindication in the bilateral performance of this procedure. On the basis of this concept our medical colleagues were consulted for approval in the application of this procedure to patients with intractable bronchial asthma who had received all known forms of specific and nonspecific therapy without relief. The protocols of three such cases are herewith presented.

CASE REPORTS

CASE 1.—D. T., No. 491774A, a white girl, 12 years of age, was admitted to the University Hospital on March 2, 1949, with a diagnosis of bronchial asthma. The family history revealed that her younger sister, paternal uncle, and maternal aunt had "hay fever." She began having asthma at the age of 5 years, shortly following tonsillectomy. Initially the attacks occurred more frequently during the summer and fall seasons, and were relieved by adrenalin and aminophyllin.

Six years prior to admission she noted a chronic cough, productive of a grayish-white, thick sputum, and three years later she was found sensitive to ragweed, eggs, and roses. Desensitization was attempted without relief. Her asthmatic attacks had so increased in severity and frequency that she was unable to attend school. During the past two years she had received the usual antibiotics, bronchodilator drugs, and antihistaminics without much relief. Change of climate was transiently effective. During this period sputum became mucopurulent and foul. She was referred to the Research Surgical Service by the allergist for consideration of surgery.

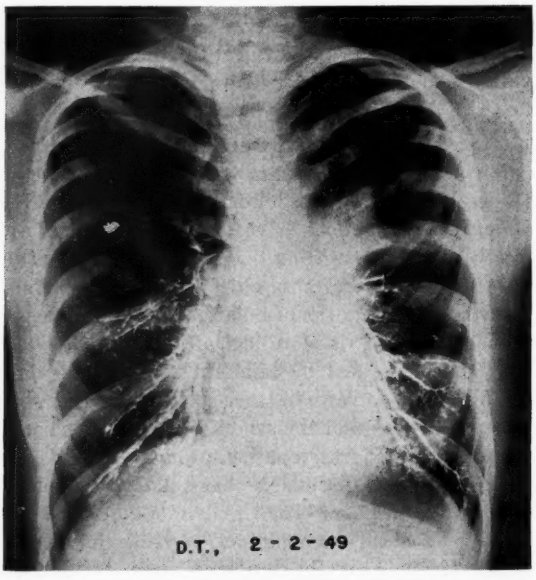
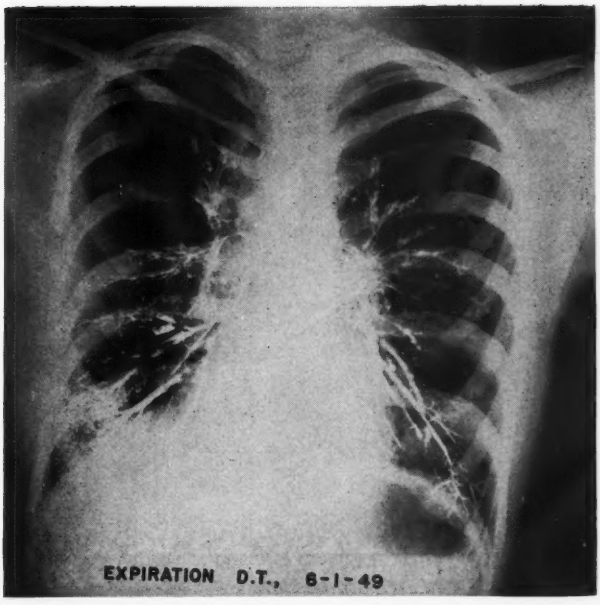


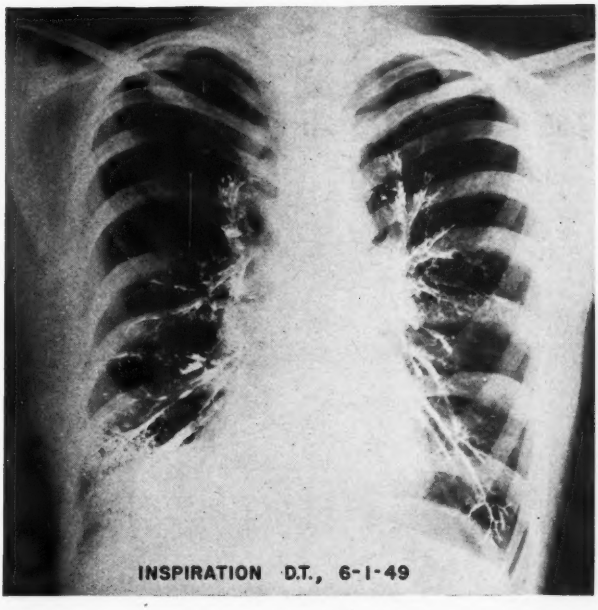
Fig. 1 (Case 1, D. T.).—Preoperative bronchogram revealing right middle lobe bronchiectasis and generalized bronchospasm of moderately severe asthma.

On physical examination her posture was drooping, the shoulders were rounded, the clavicles were raised anteriorly, and the anteroposterior diameter of the chest was increased. The sternum was prominent. There was a dorsal kyphosis. The percussion note was hyperresonant, and expiration was prolonged. Musical râles and rhonchi were heard through both lung fields. Admission white blood count was 10,500 with 5 per cent eosinophils. An electrocardiogram revealed a sinus tachycardia of 165 and right axis deviation. X-ray examination revealed the lung fields to be wide superiorly and emphysematous. A bronchogram demonstrated bronchiectasis of the right middle lobe and generalized bronchospasm (Fig. 1). The vital capacity was 1,700 c.c.

On March 7, 1949, a right posterolateral thoracotomy was performed. Continuous electrocardiographic tracings were made during the surgical procedure. Shortly after induction with Pentothal Sodium (R) endotracheal cyclopropane-oxygen anesthesia multiple extrasystoles were noted on the electrocardiogram. Upon substitution of nitrous oxide, ether and oxygen anesthesia, these changes disappeared. Exploration revealed that the lung tissue was emphysematous and the marginal veins were distended. The right middle lobe was found to be atelectatic and somewhat indurated. The right middle lobe bronchus was surrounded by enlarged lymph nodes. A right middle lobectomy was performed by the individual ligation technique, and the right vagus trunk was transected just below the origin of the recurrent laryngeal nerve. During manipulation and transection of the vagus nerve, no obvious effects



A.



B.

Fig. 2 (Case 1, D. T.).—Bronchograms obtained during expiration (*A*) and inspiration (*B*) following right vagotomy and right middle lobectomy. Comparison of the two exposures demonstrates the normal occurrence of bronchoconstriction during expiration and bronchodilatation during inspiration. Note that the same degree of generalized bronchospasm is present during both phases of respiration, and is as marked on the denervated right side as on the left.

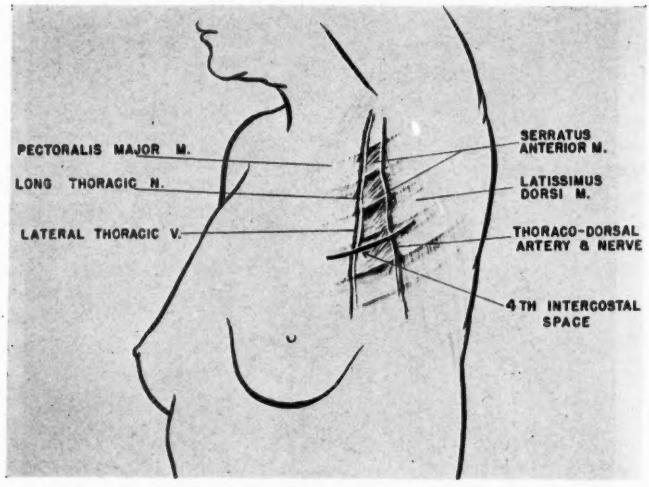


Fig. 3.—Diagram illustrating the lateral surgical approach to the vagus nerve.

Fig. 4 (Case 1, D. T.).—Roentgenogram revealing 90 per cent gastric retention six hours after the ingestion of barium.

were observed on the electrocardiographic tracings. She was discharged on the twelfth hospital day free of asthma.

Although she remained asymptomatic for three months, a bronchogram performed on June 1, 1949, revealed that bronchospasm was still present (Fig. 2, *A* and *B*). Shortly thereafter a family quarrel precipitated one of the most severe attacks that she had experienced. Following confinement to bed for three weeks she was readmitted to the hospital on June 22 in status asthmaticus. She received aerosol and systemic antibiotics, bronchodilator drugs, and chemotherapy without relief. Aminophyllin suppositories were found to be temporarily beneficial and the patient was discharged somewhat improved. On August 19, she was readmitted during a remission of her illness for consideration of left vagotomy. During an asthmatic attack the left vagus trunk was blocked in the carotid sheath with 1 per cent Novocain without relief. The admission white blood count was 10,400 with 11 per cent eosinophils. The electrocardiogram was interpreted as normal with a rate of 90. The vital capacity was 1,000 c.c.

Fig. 5 (Case 2, E. C.).—Postoperative photograph demonstrating the position and extent of the incision on the right lateral approach to the vagus nerve.

On August 24, a left thoracotomy was performed through a 15 cm. incision along the fourth interspace in the midaxillary line (Fig. 3). With the aid of lighted retractors, the vagus trunk was identified and mobilized with a nerve hook at the arch of the aorta. Since Novocain block of the left vagus trunk had been performed previously without relief, it was decided that permanent interruption of the remaining vagus nerve was not justifiable. The left vagus nerve was blocked with 1 per cent Novocain immediately below the origin of the recurrent laryngeal nerve without any discernible gross changes in the electrocardiographic tracings. Accordingly, the left vagus trunk was crushed at this point. Postoperatively she did well with the exception of complaints of epigastric fullness and bloating. An upper gastrointestinal series revealed considerable gastric dilatation, lack of peristalsis, and 90 per cent gastric retention of barium at six hours (Fig. 4). Although she remained free of asthma for a period of three weeks, gastrointestinal symptomatology increased in such severity that the administration of Urecholine, 2.5 mg. three times a day, was required. Six months after the second operative procedure, the gastrointestinal symptoms had subsided completely. There was slight but definite decrease in the frequency and severity of the asthmatic attacks. However, she required daily aminophyllin suppositories and an occasional injection of adrenalin.

CASE 2.—E. C., No. 500837A, a 57-year-old white woman, was admitted to the medical service on July 27, 1949, in status asthmaticus. She was cyanotic and comatose. This was her seventh hospital admission for the treatment of asthma.

She first had asthma during childhood; however, the attacks ceased at 12 years of age. She enjoyed relatively good health until five years prior to admission, at which time a

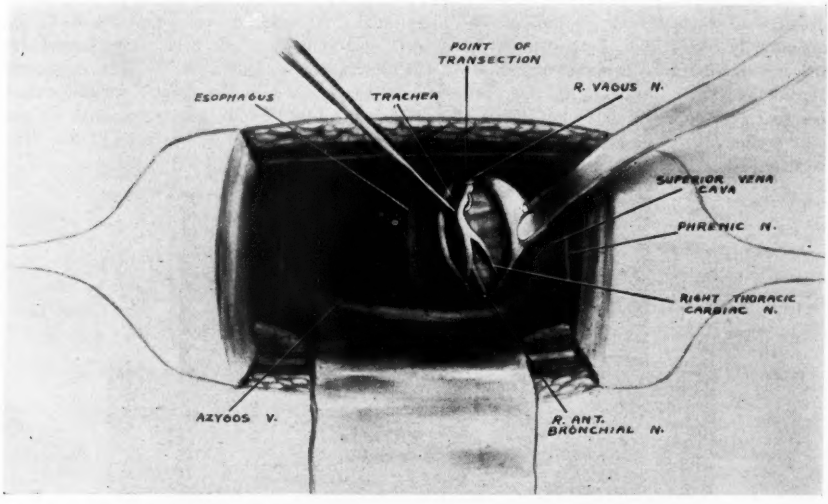


Fig. 6.—Artist's conception of the exposure of the site of transection of the right vagus nerve above the origin of the pulmonary plexus.

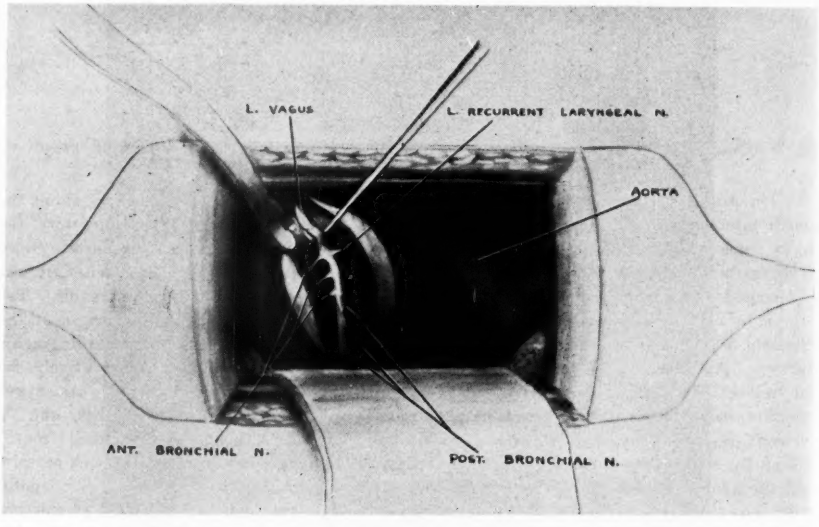


Fig. 7.—Artist's conception of the exposure of the left vagus nerve and its pulmonary branches, all of which were transected.

panhysterectomy was performed. Shortly following this procedure she noted the recurrence of asthmatic attacks characterized by sudden onset of orthopnea, sweating, and wheezing. She had been treated by many physicians. Antibiotics, bronchodilator drugs, and antihistaminics had been employed with only partial relief. Allergy studies elicited a sensitivity to house dust, cat and dog dander. Desenitization was attempted without relief. Despite additional symptomatic therapy the asthmatic attacks occurred in increasing frequency and severity.

During the seventh hospitalization, she remained in status asthmaticus for three days. After interruption of this cycle she continued to have six to eight severe asthmatic paroxysms per day, requiring various therapeutic measures. The frequency and severity of the attacks were such that the patient was afraid to leave the hospital. After forty days of hospitalization the research surgical service was requested to evaluate the patient in regard to surgery. On Sept. 8, 1949, utilizing a lateral approach (Figs. 5 and 6), the right vagus trunk was transected immediately below the recurrent laryngeal nerve. Following this procedure, the patient felt slightly improved. Some members of the staff believed there was less wheezing in the right lung than in the left. Due to the severity of the gastrointestinal symptoms in the first patient (D.T.), on September 28, only the pulmonary branches of the left vagus were

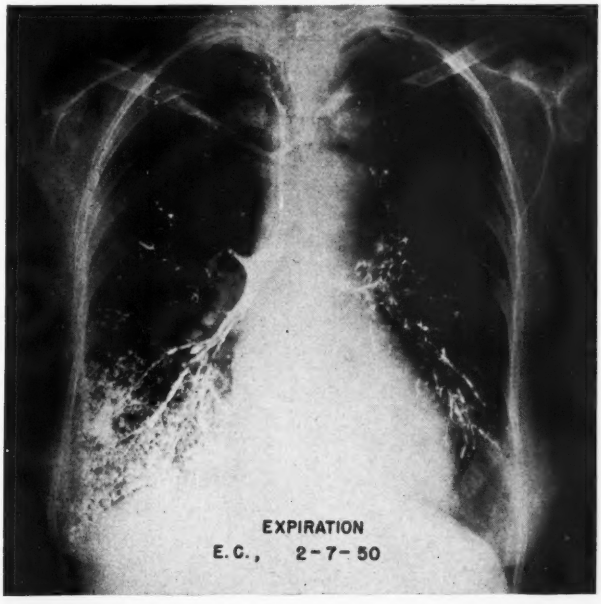


Fig. 8 (Case 2. E. C.).—Bronchogram obtained during expiration after bilateral parasympathectomy of the bronchial tree. Note the persistence of generalized bronchospasm.

sectioned, through a lateral incision (Fig. 7). The vagus trunk was not transected. The postoperative course was benign and she was discharged asymptomatic ten days after the second operative procedure. At monthly intervals examination revealed that she had remained asymptomatic, requiring no medication, and she considered herself "cured." On Feb. 7, 1950, the patient was very cheerful, stated that she felt fine and had gained fourteen pounds in weight. At this time a bilateral bronchogram was performed in order to evaluate the effect of bilateral parasympathectomy on the bronchial tree. Instillation of 8 c.c. of Lipiodol into each side of the bronchial tree precipitated a severe attack of asthma characterized by extreme dyspnea, moderate cyanosis, wheezing, and excessive perspiration. She was treated immediately in the emergency room where 7½ grains of aminophyllin were adminis-

tered intravenously and oxygen inhalation instituted. Although she was much improved after one hour, she was hospitalized overnight and discharged the following day. The bronchogram revealed severe spasm of the bronchi (Fig. 8). Since this single episode she has remained free of asthma.

CASE 3.—J. A., No. 492003A, a colored girl, 12 years of age, was first seen in the allergy clinic on Jan. 24, 1945. The following history was obtained: frequent paroxysms of coughing, shortness of breath, and wheezing had begun two years previously. Initially the attacks were more frequent during the fall and damp weather and were often precipitated by the onset of upper respiratory infection. Subsequently the attacks occurred with increasing frequency and severity, unrelated to season or weather. On occasions she noted areas of pruritis on her legs followed by welts. She had had whooping cough, measles, mumps, and chicken pox. There was no family history of allergies. At this time skin tests were negative. The vital capacity was 1,800 c.c. There were several nasal polyps; the nasal mucosa was edematous, and a mucopurulent nasal discharge was persent. The chest was emphysematous, the antero-posterior diameter being increased. Wheezing was heard throughout both lung fields.

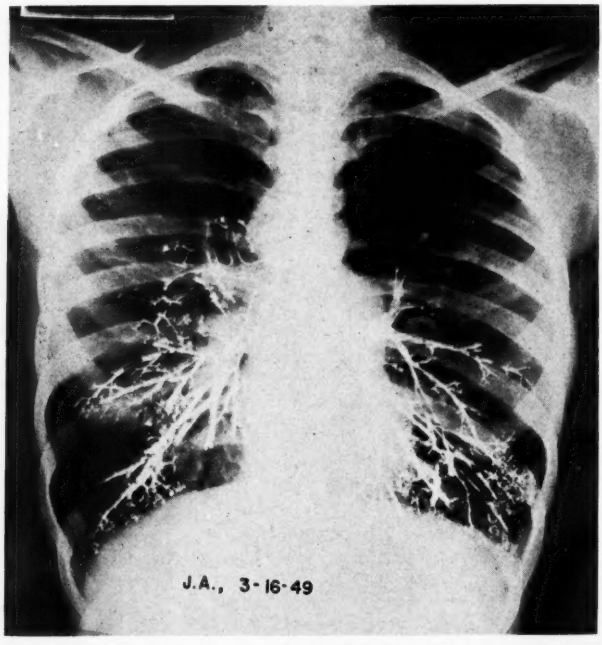
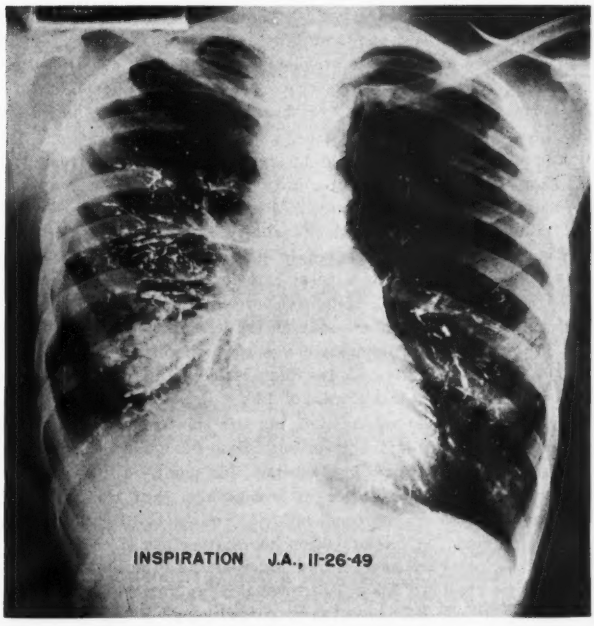
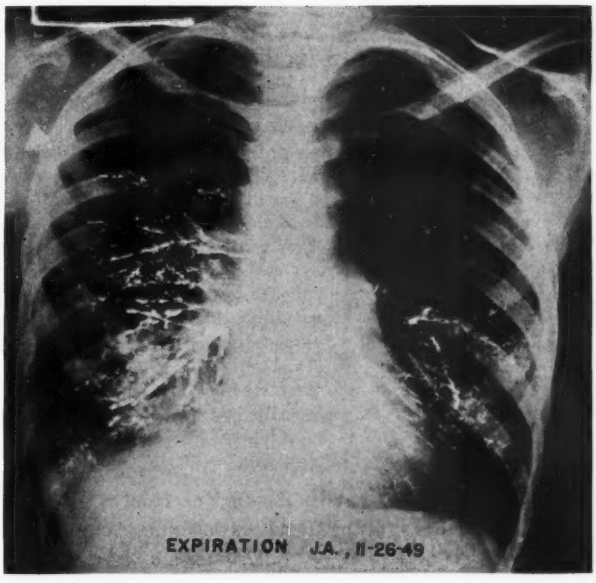


Fig. 9 (Case 3, J. A.).—Preoperative bronchogram revealing the moderate bronchospasm of asthma.

She was followed in the allergy clinic until August, 1949, on the average of two visits per month, where she had received all known specific and nonspecific therapeutic measures without relief. On her first two hospitalizations, February and March 1945, she was admitted to the ear, nose, and throat service. Multiple antrotomies were performed, and the anterior half of both middle turbinates, the polyps, and all polypoid tissue were removed. Thereafter she was followed in the ear, nose, and throat clinic, where polyps were frequently removed. On her third, fourth, and fifth hospitalizations, she was admitted to the medical service during the months of March, April, and May, 1949, for periods of seven, eight, and twenty days, respectively, in status asthmaticus. She was having four to five attacks per day, was extremely



A.



B.

Fig. 10 (Case 3, J. A.).—Bronchograms obtained during inspiration (*A*) and expiration (*B*) following bilateral parasympathectomy of the bronchial tree. Note the persistence of generalized bronchospasm during both phases of respiration.

dyspneic, incapacitated, and "adrenalin fast." There had been no weight gain in four years. The nasal mucosa was edematous and associated with mucopurulent discharge. She was round-shouldered, and there was a moderate dorsal kyphosis. The clavicles were prominent and the accessory respiratory muscles were active. The anteroposterior diameter was increased. The chest was hyperresonant and wheezes were heard throughout both lung fields. Expiration was prolonged.

Pertinent laboratory findings revealed an eosinophilia ranging from 2 to 8 per cent. Roentgenograms showed a pansinusitis and a bronchogram revealed generalized bronchospasm (Fig. 9). She was placed in an oxygen tent, received aminophyllin, grains 7½ every 3 hours, and aerosol and systemic antibiotics without relief. Status asthmaticus continued, and a surgical consultation was requested in regard to the feasibility of bilateral vagotomy. Frequent stimulation of the trachea with a nasal catheter and subsequent aspiration appeared to be responsible for interrupting the asthmatic cycle. Inasmuch as medical, allergic, and psychotherapeutic measures had been unsuccessful, she was discharged and instructed to return during a period of remission for vagotomy. She was readmitted June 1, 1949. The vital capacity was 1,300 c.c. There was a 5 per cent eosinophilia in the peripheral blood. An electrocardiogram revealed a sinus tachycardia of 130.

On June 3, using a posterolateral incision, the left chest was entered through the fourth interspace. After identification of the recurrent laryngeal nerve at the arch of the aorta, the vagus nerve was transected immediately below this point. Electrocardiographic studies revealed no effects due to vagal irritation or transection. For the first two postoperative weeks her asthma appeared to be improved, although on the third and fourth days she complained of epigastric fullness. A bilateral bronchogram performed on the tenth postoperative day revealed generalized bronchospasm on both sides of the bronchial tree. An x-ray examination of the chest twenty-four hours later revealed approximately the same amount of Lipiodol in the alveoli on the left as on the right, although a small amount of oil was remaining in one of the left lower lobe bronchi. Toward the end of her hospital stay, the attacks occurred with increasing frequency, often precipitated by conversation and diagnostic measures.

While obtaining a gastric motility tracing on her twenty-first postoperative day she had another asthmatic attack. Five minutes after injecting the right vagus trunk in the cervical region with 1 per cent Novocain, the asthmatic attack ceased. The gastric motility tracing which had been normal until this time demonstrated complete absence of peristalsis. A postoperative electrocardiogram revealed a sinus tachycardia of 110. Daily vital capacities averaged 1,100 c.c., 1,900 c.c., 1,200 c.c., and 1,400 c.c. during the first, second, third, and fourth postoperative weeks, respectively. She was discharged to return for further evaluation. No improvement was noted, and on the basis of the previous vagus injection, it was decided to cut the pulmonary branches of the right vagus nerve. She was readmitted on Oct. 31, 1949, and the operative procedure was performed as outlined in Case 2. Postoperatively she continued to have one to two attacks per day, although not as severe. Coughing paroxysms were definitely decreased. On the sixteenth postoperative day a bilateral bronchogram was performed which demonstrated a generalized bronchospasm during both the inspiratory and expiratory phases of respiration (Fig. 10, *A* and *B*). That night she had another attack of asthma, became comatose, and despite the most vigorous attempts at resuscitation, tracheal aspiration and stimulants, she died. Permission for post-mortem exmination was not granted.

DISCUSSION

A study based on three patients is insufficient from which to draw definite conclusions as to the efficacy of bilateral parasympathectomy in the surgical treatment of bronchial asthma. In addition an adequate period has not elapsed postoperatively to allow for more than a preliminary report. One patient (E.C.) states she is "cured," another (J.A.) is dead, and the remaining patient (D.T.) is slightly but definitely improved. In general, the results are only a

little better than equivocal. However, one must remember that only those asthmatic patients failing to respond to all other known measures were subjected to this operative procedure, and thus the study represents an attempt at salvage of these patients.

The most impressive finding in this investigation was the persistence of bronchospasm after bilateral interruption of the so-called "bronchomotor nerves." Regardless of the clinical result bronchospasm was demonstrable in all three patients after the instillation of Lipiodol. Bilateral parasympathectomy of the bronchial tree, thus, resulted in no change in the caliber of the bronchi. This evidence is confirmatory of our previous studies in which unilateral vagotomy performed immediately below the origin of the recurrent laryngeal nerve was without effect on the caliber of the homolateral bronchial tree. This suggests that our present concept of the neurogenic origin of bronchial asthma is not valid.

All three patients noted that cough had decreased greatly following surgery. This observation is in accordance with our previous studies in which it was demonstrated that the cough reflex arising from stimulation of the homolateral bronchial tree had been abolished following unilateral vagotomy performed above the origin of the pulmonary plexus. Since the cough reflex, the ciliary activity of the bronchial mucosa and the respiratory movements of the bronchial tree are considered to be the more important physiologic mechanisms in the maintenance of a patent bronchial tree, it must be assumed that abolition of the bronchial nerve impulses resulting in initiation of the cough reflex does not impair the efficiency of clearance of tracheobronchial secretions. Previous investigation, reviewed briefly later, revealed that unilateral vagotomy did not impair the clearance of secretions from the homolateral bronchial tree. This was demonstrated by a bronchographic study. Fortunately the patients with unilateral vagotomy serve as their own controls in that clearance of secretion from the denervated homolateral bronchial tree can be compared with the clearance of secretions from the normal contralateral bronchial tree. Caution was exercised in the performance of the bronchograms so that an equal amount of Lipiodol was introduced into each side of the bronchial tree by using a tracheal catheter. One to seven days after bronchography, posteroanterior chest roentgenograms were obtained in order to determine the residual amount of radiopaque material remaining in both sides of the bronchial tree. If the residual oil in each side was found to be of the same amount then it could be assumed that unilateral vagus section had not impaired the efficiency of clearance of secretion from the homolateral bronchial tree. With one exception there was no pooling of secretion, such as would be evidenced by a greater residuum of oil on the homolateral side. Therefore, in the absence of the cough reflex, it appears that the ciliary activity of the bronchial mucosa in conjunction with the respiratory movements of the bronchi is capable of effecting a satisfactory clearance of tracheobronchial secretions. That such is the case in the present investigation is demonstrated in the first two patients, D.T. and E.C., in whom postbronchography chest roentgenograms revealed no impairment of tracheo-

bronchial clearance following bilateral parasympathectomy of the bronchial tree. Unfortunately we were unable to obtain these studies in Case 3 (J.A.). Such studies in conjunction with a post-mortem examination would have been of the greatest importance in that investigators have reported death in asthmatics to be due to ciliary insufficiency. Hilding[24] found a metamorphosis of the normal columnar ciliated cells to goblet cells with a resultant loss of ciliary mechanism in thirty-nine fatal cases of asthma. It is logical to assume that the death of J. A. was probably due to the surgical abolition of the cough reflex in the presence of ciliary insufficiency. Because of this fact bilateral parasympathectomy of the bronchial tree should be avoided in patients having unusually severe asthma of long duration in whom metamorphosis of the normal ciliated epithelium has probably occurred. In the future, the selection of asthmatic patients to be subjected to this procedure should be made cautiously.

For a number of years investigators have demonstrated the occurrence of pulmonary edema immediately following bilateral vagotomy in experimental animals. The pathogenesis of this phenomenon has been the subject of considerable debate, and has suggested the possibility that a true "neuropathic" pulmonary edema may exist in man. That such studies do not apply to man is indicated by the absence of pulmonary edema in the preceding three cases following bilateral parasympathectomy of the bronchial tree. In addition, it is of interest that this procedure did not cause any discernible cardiovascular effects, transient or permanent, as evidenced by a comparison of electrocardiographic tracings obtained before, during, and after surgery.

In an attempt to explain the good clinical results obtained in Case 2 (E.C.) we have postulated that the occurrence of her asthmatic attacks is dependent upon the presence of two factors: a local factor (infection, hypersensitiveness, or irritation) within the bronchial tree, and a central factor. Theoretically, the local factor by itself is not capable of initiating the asthmatic paroxysm; however, in the presence of the local factor, the asthmatic attack may be precipitated by an increased number of bronchomotor impulses carried in the vagus nerve, caused by an emotional disturbance. Bilateral interruption of the nervous pathways transmitting the central factor would then inhibit the occurrence of the asthmatic attacks. Support of this theory is derived from the fact that she was free of asthma until a bilateral bronchogram was performed. Theoretically, the instillation of Lipiodol, acting as a foreign body, precipitated an attack by increasing the bronchomotor impulses through stimulation of the postganglionic vagal fibers distal to the site of previous transection.

According to the hypothesis presented earlier in this report, the ideal procedure in the surgical treatment of intractable bronchial asthma is a bilateral transection of the vagus nerves immediately below the origin of the recurrent laryngeal nerves. However, the severity of the gastrointestinal symptoms resulting from such a procedure, as in Case 1 (D.T.), does not justify its continued application. Accordingly, the surgical procedure was modified to the transection of one vagus trunk below the recurrent laryngeal nerve and the cutting of the pulmonary branches of the contralateral vagus nerve, as per-

formed in Cases 2 and 3 in two stages. No discernible gastrointestinal or cardiovascular effects were noted. At present we believe this procedure to be relatively innocuous and without any serious immediate morbidity. As pointed out previously, the application of this procedure should be made cautiously in that the selection of patients should exclude those probably having ciliary insufficiency. The possibility of performing this procedure through a unilateral approach is being considered. Although no conclusions as to the value of bilateral parasympathectomy of the bronchial tree can be made from such a small series of patients, we believe that the good clinical results obtained in Case 2 (E.C.) justify a continuation of the surgical attempts in the treatment of intractable bronchial asthma.

SUMMARY

1. A review of the literature pertinent to the anatomy and physiology of the extrinsic pulmonary nerves as related to bronchial physiology is presented.

2. The present concept of the pathologic physiology of bronchial asthma as related to its neurogenic origin is discussed.

3. The surgical procedures previously performed by various investigations on the extrinsic pulmonary nerves in cases of intractable bronchial asthma are briefly reviewed.

4. Three patients with intractable bronchial asthma were subjected to bilateral parasympathectomy of the bronchial tree. Although the clinical results are little better than equivocal, bronchospasm was still present in all three patients as demonstrated by bronchography.

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(See discussion on page 591.)

THERAPEUTIC STATUS OF PULMONARY AUTONOMIC NERVE SURGERY

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THE possible application of surgery of the autonomic nervous system to bronchial asthma has long been considered and sporadically applied. Such procedures as stellate ganglionectomy[1] and high dorsal sympathetic nerve block[2] have been suggested for application in this disease since 1923. Rienhoff and Gay[3, 4] reported promising results following procedures attempted toward complete denervation of the lung by excision of the posterior pulmonary plexus in 1938. In 1947, Carr and Chandler[5] presented the long term results following dorsal sympathectomy for bronchial asthma. In the discussion of this paper, the possible value of autonomic surgery in other pulmonary conditions such as emphysema[6] was considered. Blades,[7] in 1948, presented a review of the history of the surgical approaches utilized in bronchial asthma and presented the early results of a considerably more radical method of pulmonary denervation in the surgical management of this disease. Bailey[8] has also stressed the importance of more radical measures. A distinct contribution to our knowledge of the physiologic effect of the vagus upon the bronchial tree has recently been presented by Curtis and Klassen.[9] They have demonstrated the transmission of sensations of bronchial discomfort along vagal pathways and have applied this knowledge in the utilization of high vagus transection as a palliative measure for the intractable cough of nonresectable bronchiogenic carcinoma.

We are not as yet in full possession of a knowledge of the role which the autonomic nervous system plays in regard to bronchial physiology. It is admittedly difficult or impossible to apply experimental studies upon the autonomic nervous system of animals to a satisfactory understanding of the physiology of this nervous system in the human being. The reported results of surgery of the autonomic nervous system in the treatment of bronchial asthma in the human being have so far been unable to show any true uniformity.

The surgery of the dorsal sympathetic chain has been quite comparably done by different authors. However, when one studies the reports relative to attempts at complete pulmonary denervation, it becomes obvious that there is a considerable discrepancy in the completeness with which this procedure has been carried out. Certainly prior to 1947 there had not been satisfactory recognition of the number and importance of fibers going from the vagus nerve to the pulmonary hilus from a level at and above the recurrent laryngeal nerve. The experiences of ourselves and others make us feel that considerable stress

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should be laid upon the fibers which may descend to the hilus from the recurrent laryngeal nerve itself and also those which arise from the main vagal trunk above the recurrent laryngeal nerve. In the main, these fibers tend to go to the anterior portion of the hilus and particularly are distributed in the tissues about the pulmonary artery and superior pulmonary vein. Blades has emphasized the number of sympathetic nerve fibers which may come across from the contralateral side of the chest via the pulmonary artery. He also emphasized the frequency with which both vagal and sympathetic fibers may enter the lung route through the pulmonary ligament. It is vitally important, therefore, in any consideration of the application of autonomic surgery to pulmonary disease that the specific degree of completeness of pulmonary denervation be emphasized. In 1945, we felt that we were carrying out a more complete denervation of the lung when we were severing the higher fibers from the vagus and cleaning the hilus down to the level of the pulmonary ligament. However, we now know that this is an incomplete pulmonary plexectomy or denervation and prior to 1949 we can only find one of our patients in whom we can consider that a truly complete plexectomy had been carried out. That was in 1945, when we first added perivascular sympathectomy and complete transection of the pulmonary ligament. In retrospect we find that we had much more benefit in this individual patient.

We feel, therefore, that it is important to classify the denervation procedures in four separate categories. First, there is dorsal postganglionic sympathectomy involving the removal of the second through the fifth and occasionally through the seventh sympathetic ganglia. Second, there is transection of the vagus nerve just below the level of the recurrent laryngeal nerve which must admittedly leave even some distinct fibers of the vagus going into the pulmonary hilus; this we call "high vagus transection." Third, there is the operation of completely transecting all visible fibers of the vagus going into the hilus of the lung except for those going through the pulmonary ligament and without stripping of the sympathetic fibers coming through the perivascular sheaths; this procedure we will classify as "partial or incomplete pulmonary plexectomy." Finally, there is the most complete type of pulmonary denervation, that described by Dr. Blades, which we classify as "complete pulmonary plexectomy or denervation."

The attacks upon the sympathetic, parasympathetic, and combined autonomic nervous systems have made us feel that a comparative study of the results of the application of these different methods in one clinic might prove valuable in a further understanding of this subject. In the discussion of Dr. Carr's paper before this Society in 1947, both Dr. Ralph Adams and one of us (O. A. A.) drew attention to instances of apparent benefit of autonomic surgery in relation to pulmonary emphysema. We have tried to apply autonomic surgery in other types of pulmonary disease and wish to consider the role of such an approach in these other diseases at this time. To date we have carried out autonomic nerve surgery as a solitary procedure or in conjunction with other surgical procedures in relation to pulmonary disease in 72 patients.

We are fully cognizant of the difficulty in evaluating the results of autonomic surgery in relation to pulmonary disease. In patients with severe dyspnea or with asthma there is almost constant associated personality disturbance. It is frequently difficult or impossible to determine whether this personality disturbance anteceded the pulmonary difficulty or presented as a consequence of prolonged pulmonary disability. We have attempted in all cases to evaluate the personality status and in almost all patients have carried out a prolonged trial of conservative measures directed toward (1) reassurance with psychotherapy, (2) improvement in associated pulmonary suppuration by endoscopy under ether anesthesia, chemotherapy, chest exercises, and expectorants, and (3) improvement in the breathing habits, particularly by expiratory chest exercises. In many instances there has been a striking result from this conservative type of approach. No patient was subjected to autonomic surgery until we were satisfied that this type of approach had failed. One must also emphasize that in the application of a procedure which is not necessarily an accepted one the caliber of patients treated consisted in the main of those with very far advanced and intractable disease.

As our experiences have grown with the application of these procedures we have become increasingly impressed with the need for objective studies in regard to pulmonary function both before and after surgical interference. Adequate pulmonary functional studies have only recently been available to us, and we feel that further experience with this method of study and of longer follow-up of these objectively studied patients should be carried out before presenting specific results from this more objective approach. For the past five years we have tried to apply an admittedly very limited method of study in regard to these patients; namely, to study the effect of various drugs upon the individual's vital capacity before treating the patient either by the conservative or combined conservative and surgical approach. The only value noted in this study is that we have been impressed by the considerable increase in vital capacity in patients with bronchial asthma following injection of epinephrine, Isuprel, or aminophylline, and it also appears to be an essentially uniform finding in the study of patients with extensive bilateral emphysema. More detailed studies are being carried out by the pulmonary function laboratory to investigate further the role of associated bronchospasm in pulmonary emphysema. At present, we must state that we cannot accept the premise that bronchospasm is not an important and probably integral part of diffuse interstitial or bullous emphysema or a combination of those types of emphysema.

CLINICAL OBSERVATIONS

1. Bronchial Asthma.—Having been stimulated by Dr. Carr's observations in 1947, we began a series of patients with different types of autonomic surgery in an attempt to control intractable bronchial asthma. The procedures utilized consisted of (1) upper dorsal postganglionic sympathectomy, (2) high vagotomy, (3) plexectomy which we then thought was complete and now must consider as partial or incomplete plexectomy, and (4) a more recent group

applying the complete plexectomy procedure. It must be stressed that certain postoperative mortalities which occurred early in this study appear to have been avoidable in view of subsequent experience. Patients with intractable bronchial asthma present a difficult physiopathologic entity to treat, and it would appear important to discuss these early deaths and the experiences obtained therefrom.

In one patient there was produced a contralateral tension pneumothorax during the operative procedure which in retrospect can probably be attributed to considerable difficulty in anesthesia induction. Any anesthetic agent prone to produce bronchospasm must be avoided in asthmatic patients. The particular drugs to avoid are sodium pentothal and cyclopropane. The use of a good basal anesthetic such as rectal ether or avertin has met with considerable improvement in regard to anesthesia induction in our experience. This patient with a tension pneumothorax on the contralateral side died twelve hours postoperatively during the insertion of a thoracentesis needle. The actual cause of death was attributed to air embolism. In two other patients there was an acute obstructive type of emphysema, and since we were reluctant at that time to bronchoscope this group of patients, they did not undergo what we feel from autopsy findings would have been a life-saving bronchoscopy. We feel that it must be stressed that the bronchoscope is an almost routine measure in the postoperative course of these patients. In a further instance a patient who had undergone an initial procedure on the left side with a fairly good immediate result died following the operation upon the second side carried out after a four-month interval, due to improper handling of a postoperative cardiac arrhythmia. This patient developed a rather severe auricular fibrillation and was given 0.8 mg. of Cedilanid intravenously and this rhythm converted to a ventricular tachycardia. A second dose of 0.8 mg. of Cedilanid intravenously was given in the presence of this type of rhythm with immediate transformation of the ventricular tachycardia into a fatal ventricular fibrillation. It must be stressed that pre- and postoperative electrocardiograms are of considerable value in the handling of postoperative complications in this patient group. Two other deaths occurred in this series; both of these patients were over 70 years of age with completely intractable asthma. Each patient had shown a poor response following sympathectomy on one side and died following the operation upon the contralateral side. Both these patients had marked pulmonary destruction and suppuration and also advanced coronary heart disease. In retrospect, one must consider that despite the apparent hopeless situation that these patients were too severe risks for the operative procedure.

A. Results in the Surgical Treatment of Bronchial Asthma With Sympathectomy Alone: The results obtained in the application of upper dorsal postganglionic sympathectomy in a group of fourteen patients with intractable bronchial asthma are presented in Table I. In this group of patients, 5 were subjected to bilateral sympathectomy, 2 of whom died and consist of the 2 aged patients previously mentioned. These 2 patients and one other who has been followed for approximately twenty-two months must be considered as

TABLE I. BRONCHIAL ASTHMA—SYMPATHECTOMY ALONE

NUMBER OF PATIENTS		RESULTS				
		FAILURE	FAIR	GOOD	CURED	DEATHS
Left Side	7	2	3	0	2	0
Right Side	2	0	0	0	2	0
Bilateral	5	3	2	0	0	2
Total	14	5	5	0	4	2*

*Deaths are included in failures.

complete failures. The 2 patients who died were observed for three- and four-month intervals between operations, and no satisfactory response had been obtained from the initial procedure. Two patients had upper dorsal post-ganglionic sympathectomy on the right side only and both of these patients have shown a very satisfactory follow-up completely free of asthma eighteen and twenty-six months, respectively. Seven patients were subjected to a left upper dorsal sympathectomy alone. This group has produced two complete failures with persistent asthma of equal severity to that before operation. Three have had fair results in which the degree of asthma has been decreased at least 50 per cent, and 2 have continued to be completely free from asthma for twelve and fifteen months, respectively.

This group of patients was then re-evaluated as shown in Table II to try to find a common denominator in regard to those patients who had a failure, a fair or good result, and those who had become asthma-free. In every instance it was found that those who had become cured or free of their asthma did not have major associated pulmonary suppuration or destruction. In those having such major suppuration there were four complete failures and four in whom the result could be classified as only fair. In this group repeated chemotherapy has been utilized to help control the postoperative situation and must receive a considerable proportion of the credit for the "fair" group of results. Three patients undergoing this procedure, who presented a complete failure post-operatively, were serious narcotic addicts in whom the addiction could not be controlled either before or after operation. The 4 patients who obtained apparent complete cure were derived from a group who had associated disease in the thorax and who required an intrathoracic procedure essentially for this associated disease and the sympathectomy was carried out in conjunction because of known associated moderately severe or severe bronchial asthma. The 4 patients who could be classified as cured had sympathectomy of unilateral type

TABLE II. BRONCHIAL ASTHMA—SYMPATHECTOMY ALONE
(ROLE OF ASSOCIATED DISEASE)

	NO. OF PATIENTS	RESULTS		
		FAILURE	FAIR	CURED
Diffuse Suppuration	8	4	4	0
Narcotic Addiction*	3	3	0	0
Miscellaneous Disease†	6	1	1	4
Total	14	8	5	4

*Two narcotic addicts had diffuse suppuration.

†Carcinoma of esophagus; emphysema; cardiospasm; neurofibroma; carcinoma lung, peripheral; carcinoma, lung, with suppuration.

in conjunction with (1) an operation for cardiospasm, (2) another with a posterior mediastinal tumor, namely a neurofibroma, (3) another had a peripheral type of inoperable pulmonary carcinoma, (4) while the other had an esophageal resection for primary carcinoma of that organ. The patient with inoperable pulmonary carcinoma lived for five months without any recurrence of what previously had been constant bronchial asthma. The patient having cardiospasm had had intractable asthma for two years prior to operation and has remained completely free of asthma for eighteen months. The patient in whom a neurofibroma was removed had not been free of asthma for forty-three years prior to operation and has remained free of asthma now for nineteen months. The patient having a resection of the esophagus for carcinoma has been observed fourteen months postoperatively, and he is completely relieved of bronchial asthma which had been constantly present for twenty-two years previously. One patient in whom the result can be classified as a failure had a bronchiogenic carcinoma with considerable suppuration and continued to have constant asthma for seven months following the procedure. One patient having a fair result had most extensive pulmonary emphysema and also diffuse suppurative disease. It is our impression, therefore, from this patient group that a good result cannot be obtained from sympathectomy alone in patients having diffuse destructive pulmonary suppuration. An equally hopeless group is the patient having bronchial asthma who has become a severe narcotic addict. The happiest results from sympathectomy appear to be those in whom no suppurative disease has occurred.

B. Surgical Treatment of Bronchial Asthma by the Use of Varying Degrees of Pulmonary Plexectomy: Results obtained by the use of attempts at pulmonary denervation or by transection of the vagus nerve just below the level of the recurrent laryngeal nerve are presented in Table III. There were 18 patients in this group. Two patients had high transection of the vagus, and the results in both these patients were essentially unsatisfactory and at best can be classified as fair. With the application of partial or incomplete plexectomy or denervation there were 12 patients subjected to this procedure. Four of these patients died within the first three weeks following operation and a fifth died without relief of asthma ten weeks following surgery. This last-mentioned patient had severe associated diffuse pulmonary suppuration and obtained no benefit whatsoever from the procedure. One patient having a partial plexectomy was distinctly improved and has been followed over one year after

TABLE III. BRONCHIAL ASTHMA—PLEXECTOMY OR VAGOTOMY

PROCEDURE	NO. OF PATIENTS	RESULTS				
		DEATHS	FAILURE	FAIR	GOOD	CURED
High Right Vagotomy	2			2		
Left	1	1				
Partial Plexectomy						
Left	9	2	4	1	2	
Bilateral	3	1	1		1	
Complete Plexectomy						
Left	3			1	1	1
Total	18	4	5	4	4	1

surgery; the severity and frequency of asthmatic attacks have been considerably attenuated. The 3 patients in this group classified as good results could be classified in the cured group except for rare extremely mild asthmatic attacks not requiring drugs in two instances and only rarely requiring drugs in the other. The 3 patients undergoing complete pulmonary denervation according to the methods of Blades have shown much better results. One is apparently cured, 1 is very markedly improved with rare asthma attacks, and the one patient having only a fair result has associated diffuse pulmonary suppurative destruction.

C. Surgical Treatment of Bronchial Asthma by Means of Autonomic Nerve Surgery Plus Resection of "Trigger Areas." (See Table IV): It has been the experience of the authors to encounter 13 patients in the past three years who had severe bronchial asthma in association with demonstrable localized areas of pulmonary destruction. It is felt from clinical experience with this group that these localized areas in some way played a productive role in relation to the patient's bronchial asthma and have therefore been classified as "trigger areas." Prior to this group we had experience with lobectomy for bronchiectasis in 5 patients having associated bronchial asthma in whom the bronchial asthma persisted following the operative procedure. In this group of 13 patients, 8 underwent some form of sympathectomy in association with segmental pulmonary resection or total lobectomy. There were none in this group which could be classified as a complete failure in regard to the effect of the operative procedure upon the patient's associated bronchial asthma. Three had a result which could be classified as only fair; 2 of these had bilateral bronchiectasis with bilateral segmental resection but the sympathectomy was confined to one side. The third in this group of fair results is a severe frank psychotic. Two patients having good results with resection of "trigger areas" plus a left dorsal postganglionic sympathectomy have had very rare attacks of asthma following operation not requiring drugs. One patient with bilateral bronchiectasis undergoing bilateral surgery had concomitant bilateral sympathectomy with an apparent cure. In all those patients achieving an apparent cure in this group there has been complete removal of demonstrable areas of pulmonary destruction. One patient had a right upper lobectomy for bronchiectasis and an associated high right vagus nerve transection because of antecedent severe bronchial

TABLE IV. BRONCHIAL ASTHMA—AUTONOMIC SURGERY PLUS RESECTION OF TRIGGER AREAS*

	NO. OF PATIENTS	RESULTS			
		FAILURE	FAIR	GOOD	CURED
Sympathectomy					
–Right	2		1		1
–Left	5		2	2	1
–Bilateral	1		0		1
High Right Vagus Resection	1			1	
Complete –Right	1				1
Plexectomy –Left	3				3
Total	13	0	3†	3	7

*Eleven of these patients had associated segmental resection or total lobectomy for bronchiectasis. Three had excision of major localized tension bullae.

†Two of this group have suppurative disease still present on the contralateral side. One patient is frankly psychotic.

asthma, and she has been followed for twenty-six months and has had only two extremely mild attacks of asthma during that interval. Four patients have been subjected to resection of apparent "trigger areas" along with complete pulmonary denervation and in all 4 of these patients an extremely satisfactory result has been obtained. Of the 13 patients in this group, 11 had their "trigger areas" consisting of pulmonary segments or lobes destroyed by bronchiectasis. The two remaining patients had local areas of major emphysematous bullae.

In summary (see Table V) we present experience with 45 patients with severe bronchial asthma in whom autonomic surgery or a combination of autonomic surgery plus removal of "trigger areas" of pulmonary destruction have been carried out. The most beneficial results have been obtained in the patient group in whom resection of areas of pulmonary destruction plus a complete pulmonary denervation has been performed. Markedly beneficial results have been obtained in those patients having removal of "trigger areas" of pulmonary destruction plus either parasympathetic or sympathetic interruption. If the operative procedure is to be confined purely to the interruption of the autonomic nervous system, the patient should neither have evidence of serious diffuse suppurative pulmonary destruction, nor have evidence of major associated psychic disturbance such as narcotic addiction.

TABLE V. BRONCHIAL ASTHMA—COMPARATIVE RESULTS FOLLOWING DIFFERENT SURGICAL PROCEDURES

PROCEDURE	NO. OF PATIENTS	RESULTS			
		FAILURE	FAIR	GOOD	CURED
Dorsal Sympathectomy	14	5	5	0	4
Partial Plexectomy	15	9	1	3	0
Complete Plexectomy	3	0	1	1	1
Sympathectomy plus Excision Area Lung Destruction	8	0	3	2	3
Partial Plexectomy plus Excision Area Lung Destruction	1	0	0	1	0
Complete Plexectomy plus Excision Area Lung Destruction	4	0	0	0	4
Totals	45	14	10	7	12

2. Pulmonary Emphysema.—

The authors are in the process of carrying out objective studies in a group of patients with severe pulmonary emphysema either of the primarily bullous type or of the interstitial type of emphysema. It is felt too early to be able to present objective results in this group of patients, but the preliminary clinical results of this group are presented in Table VI. Several of these patients can be classified to have what is termed "vanishing lung disease" and a satisfactory evaluation of this group will have to be done both in regard to symptomatology, objective studies, and the future progress of the underlying "vanishing lung disease." We are able to state at the present time that symptomatic cure has been obtained in four patients having autonomic surgery in association with resection of major bullae and in these patients at operation there was found

TABLE VI. PULMONARY EMPHYSEMA

PROCEDURE	NO. OF PATIENTS	DEATH	FAILURE	FAIR	GOOD	SYMPTOMATIC CURE
Sympathectomy						
–Left				2	1	
–Right						
–Bilateral			1		2	
Plexectomy						
–Left Partial						
–Left Complete						
–Right Complete						
Bullae						
–Sympathectomy						2
–Partial Plex.					1	2
–Complete Plex.				1		
Total	12	0	1	3	4	4

to be associated diffuse interstitial emphysema. Four patients have apparently good results from left sympathectomy in one, bilateral upper dorsal sympathectomy in two, and partial pulmonary denervation plus removal of emphysematous bullae in one. Three patients have shown only fair results to date, and one must be characterized as a frank failure. It is felt that further objective investigation and further follow-up will be required in this group before being able to present any conclusions. It is important to stress that we do feel that we see a considerable amount of bronchospasm in association with extensive emphysema and that occasional patients apparently benefit from autonomic nerve surgery in this disease. It is also felt that some patients with major emphysematous bullae will benefit by using some denervation procedure in conjunction with resection of the bullae if there is preoperative evidence of major bronchospasm.

3. Autonomic Surgery as a Palliative Measure in Inoperable Bronchiogenic Carcinoma.—

The results of the application of different types of autonomic surgery in patients who, on exploratory thoracotomy, were found to have inoperable carcinoma of the lung are presented in Table VII. There are 10 patients in this group. In 1946 and 1947, we carried out upper dorsal sympathectomy at the conclusion of the exploratory operation in 6 patients and during the follow-up period achieved no benefit in regard to severe cough in 5 of these patients. In 1 patient there appeared to be a considerable benefit in regard to cough, but this patient also had associated bronchial asthma, and this symptom was apparently relieved by the operative procedure. Since 1948, we have utilized high vagus resection in 4 patients with bronchiogenic carcinoma and

TABLE VII. INOPERABLE BRONCHIOGENIC CARCINOMA—EXPLORATION PLUS AUTONOMIC SURGERY

PROCEDURE	NO. OF PATIENTS	EFFECTIVE PALLIATION	NO PALLIATION
Sympathectomy	6	1*	5
High Vagus Resection	4	4	0
Total	10	5	5

*This patient had asthma and was relieved for five months.

have appeared to obtain effective palliation in regard to cough in each patient of this group. It is our impression, therefore, from a study of these 10 cases that upper dorsal sympathectomy does not have any usefulness as a palliative measure in regard to cough, while high vagus resection can be of considerable value. It should be noted that we have seen 3 patients with bronchiogenic carcinoma in whom at autopsy the vagus nerve on the involved side had undergone complete destruction, and these patients' terminal courses were rather strikingly free of intractable cough.

4. Role of Associated Autonomic Surgery Along With Pulmonary Resection in Certain Cases of Bronchiectasis.—

To date the authors have tried the application of autonomic nerve surgery in association with pulmonary resection in a group of 14 patients with bronchiectasis. The patients with bronchiectasis in whom this operative procedure was considered were only those patients with bronchiectasis showing a major degree of associated allergy and bronchospasm. Many of these patients had actual asthmatoid attacks, but those we did not classify as true asthma. There was marked evidence on clinical examination of diffuse bronchospasm which was also shown on bronchogram. It had been our experience to have several patients of this type in whom lobectomy had been carried out and who had palliation of the major bronchiectatic symptoms but continued to have some wheeze, some bronchorrhea, and other complaints apparently referrable to allergy and bronchospasm. In this group of patients (see Table VIII) upper dorsal sympathectomy was carried out in association with lobectomy in eleven. A satisfactory beneficial result was obtained in 9 while the 2 patients classified either as a failure or as fair had bilateral disease and bilateral resection but only unilateral sympathectomy. The patients having most satisfactory results were 4 who had unilateral bronchiectasis with associated unilateral sympathectomy and 3 who had bilateral resection associated with bilateral autonomic surgery. It is our impression from this group that this type of patient does benefit by autonomic nerve surgery either of sympathectomy or pulmonary plexectomy type, and if the patient has bilateral disease then bilateral autonomic nerve interruption should be carried out.

TABLE VIII. BRONCHIECTASIS—PLUS DIFFUSE BRONCHOSPASM AND ALLERGY (PULMONARY RESECTION PLUS AUTONOMIC SURGERY)

PROCEDURE	NO. OF PATIENTS	RESULTS			
		FAILURE	FAIR	GOOD	CURED
Sympathectomy	11	1*	1*	4	5
Partial Plexectomy	3			1	2
Total	14	1	1	5	7†

*These patients had bilateral segmental resection but autonomic surgery only on one side.
†Three of the seven patients cured had bilateral resection and bilateral autonomic surgery.

5. Sympathectomy in the Treatment of Severe Bronchorrhea.—

Results in 2 patients having severe bronchorrhea in whom upper dorsal sympathectomy was carried out are presented in Table IX. These patients both had very copious production of sputum with considerable associated wheez-

ing. Results in these 2 patients following sympathectomy appear to be quite striking in the reduction of the 24-hour sputum production. These 2 patients are presented purely as a matter of interest only, and further study of this patient group will be required before making any conclusions.

TABLE IX. SYMPATHECTOMY FOR BRONCHORRHEA

TYPE	NUMBER OF PATIENTS	PRODUCTION BEFORE SURGERY	PRODUCTION AFTER SURGERY	DURATION FOLLOW-UP
Unilateral Left D1-7 R 2-5	1	14 oz./24 hr.	3 oz./24 hr.	18 mo.
Bilateral L 2-6	1	24 oz./24 hr.	1½ oz./24 hr.	7 mo.

6. Autonomic Surgery in Conjunction With Decortication and Reconstructive Procedures in the Treatment of Chronic Recurrent Pneumothorax.—

Table X presents the results in 5 patients who were treated by the removal of bullae, overlying peel, and associated autonomic nerve surgery for chronic recurrent spontaneous pneumothorax. The roentgenograms on all 5 of these patients showed considerable associated bilateral emphysema of the interstitial type. These patients, in all instances, had small bullae on the side of operation which were felt to be the responsible agent for the recurrent pneumothorax. The addition of autonomic nerve surgery was carried out because of the appearance of the lungs on the x-ray studies as well as the diffuse emphysematous appearance of the lung on the operative side. In all instances these patients showed some demonstrable objective evidence of bronchospasm prior to the operative procedure, and this was also considered as part of the rationale for the addition of the autonomic nerve surgery to the other procedures. This group of patients is again too small to draw any conclusions, but the results appear to be good, and there appears to have been in each instance a considerable decrease in regard to subjective dyspnea which was present between episodes of pneumothorax or prior to the onset of the initial pneumothorax. The major reason for considering this type of procedure is in regard to its possible application for the treatment of pulmonary emphysema.

TABLE X. CHRONIC RECURRENT PNEUMOTHORAX—RECONSTRUCTIVE PROCEDURES PLUS AUTONOMIC SURGERY

PROCEDURE	NUMBER OF PATIENTS	RESULTS			
		FAILURE	FAIR	GOOD	RELIEF FROM PNEUMOTHORAX AND DYSPNEA
Bullae sympathectomy	1				1
Bullae plexectomy	4			2	2
Total	5			2	3

SUMMARY

The authors present their experience with 72 patients in whom some form of autonomic nerve surgery has been applied in relation to pulmonary disease.

Forty-five of these patients were treated for bronchial asthma, and a comparison of the result obtained with sympathectomy, partial or complete plexectomy, and a combination of autonomic surgery plus the removal of "trigger areas" of pulmonary destruction has been presented. Experience with 10 patients utilizing either a sympathectomy or parasympathectomy as a palliative measure in bronchiogenic carcinoma has suggested that parasympathectomy may be of palliative value in this disease. This would appear to confirm the experiences of Curtis and Klassen. A group of patients in whom autonomic surgery has been utilized as a solitary procedure or in conjunction with reconstructive procedures in pulmonary emphysema has been noted. It is the authors' experience that pulmonary emphysema does involve considerable associated bronchospasm. A group of patients with bronchiectasis in whom there was major associated bronchospasm and allergy but who did not have actual asthma is also discussed in regard to the effectiveness of combining autonomic nerve surgery along with pulmonary resection. Five patients having chronic recurrent spontaneous pneumothorax and subjected to reconstructive procedures plus autonomic surgery are described. Finally, 2 patients are noted with severe bronchorrhea, who obtained beneficial results from sympathectomy. Another patient, treated three years ago, had repeated spontaneous pulmonary thromboses on one side, one of which progressed to actual abscess destruction of the right middle lobe. This patient was treated by right middle lobectomy plus dorsal sympathectomy, in view of the presence of arteriolar disease at the time of frozen section. This patient has continued well for three years, but the role of autonomic surgery in this individual patient cannot be evaluated in view of the fact that this patient has also been kept on constant Dicumarol therapy.

CONCLUSIONS

It is our opinion, therefore, from a presentation of the preceding clinical experiences with 72 patients undergoing different types of pulmonary autonomic surgery, that:

1. Distinct beneficial results can be obtained from autonomic nerve surgery in certain types of pulmonary disease, but

2. Considerable objective data by means of pre- and postoperative respiratory function studies will be needed before final conclusions can be made.

However, on the basis of clinical evaluation alone, our experiences suggest that:

3. Autonomic surgery, alone, in the form of complete pulmonary plexectomy or denervation, should be markedly beneficial in the treatment of intractable bronchial asthma unless there is evidence of associated suppurative pulmonary destruction, narcotic addiction, or major psychosis.

4. Autonomic surgery, preferably in the form of complete pulmonary plexectomy, plus excision of "trigger areas" of pulmonary destruction can be markedly beneficial or curative in the treatment of intractable bronchial asthma.

5. The only autonomic surgery of palliative value in the treatment of advanced bronchiogenic carcinoma consists of transection of the parasympathetic fibers (vagus nerve).

6. Bronchospasm plays an important role in the progress of pulmonary emphysema, and autonomic surgery can be of value in the surgical treatment of this disease, particularly as an adjunctive measure to the resection of major bullae.

7. Autonomic surgery in addition to pulmonary resection should be considered in certain bronchiectatic patients with associated marked allergic and bronchospastic tendencies. If such patients require bilateral pulmonary resection, then bilateral associated autonomic surgery is required.

8. Two patients with severe idiopathic bronchorrhea treated by upper dorsal sympathectomy are reported. In both instances marked relief from bronchorrhea was obtained.

9. Autonomic surgery is considered a valuable adjunctive measure in the operative correction of chronic recurrent spontaneous pneumothorax where there is associated interstitial emphysema.

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(See discussion on page 591.)

THE SURGICAL TREATMENT OF INTRACTABLE ASTHMA

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DURING the past thirty-four months 38 patients have been operated upon for severe asthma at the George Washington University Hospital. These cases were selected from approximately 300 patients complaining of the disease. The 38 cases subjected to surgical intervention were completely incapacitated and all known conservative treatment had failed. There were 14 women and 24 men. Their ages varied from 15 to 72 years. The majority of the patients were in the third to the fifth decades of life.

Operations for Asthma.—Kümmell,[1] in 1923, operated upon the sympathetic nervous system for the treatment of severe asthma. His early results appeared to be satisfactory. Approximately one year later, Kappis[2] was equally optimistic about the results of vagotomy for asthma. He divided the vagus on the right side below the level of the recurrent laryngeal nerve. Other surgeons in the past have employed varying techniques for operations on both the sympathetic and parasympathetic systems. Leriche and Fontaine[3] advocated stellate ganglionectomy; and combined operations involving sympathectomy and unilateral vagotomy were employed by Kümmell[1] and others.

Modern revivals of operations on the autonomic nervous systems include Carr and Chandler's[4] reports on the role of dorsal sympathetic ganglionectomy for asthma, Phillips and Scott's[5] use of operations on the parasympathetic system, and later Rienhoff and Gay's[6] contributions concerning bilateral posterior pulmonary plexus resection.

An operation based on the same general approach employed by Phillips and Scott[5] and later by Rienhoff and Gay[6] has been performed in our series.

A left posterolateral incision is made over the fifth rib and after division of the overlying muscles a long segment of the rib is resected. The pleura is incised and the left thoracic cavity opened.

The operation consists of the following steps: 1. Identification of the vagus nerve at the level of the pulmonary plexus. 2. The vagus is freed and retracted gently, but not cut. 3. The pulmonary plexus about the bronchus is destroyed. 4. All branches of the vagus to the pulmonary hilum and lung are divided below the level of the recurrent laryngeal nerve. 5. The esophageal branches and the main trunk of the vagus are saved. 6. The sheaths of the pulmonary artery and veins are removed as much as possible. 7. The pulmonary ligament is divided.

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The chest wall is reconstructed in layers with an intercostal catheter placed in a separate stab wound and connected to a water-sealed bottle.

There are considerable variations in the patterns of the vagus nerve distribution to the lungs. Observations during 44 operations and dissections on 12 fresh cadavers revealed that the nerve supply to the left lung is considerably greater than the right. On the left side one can usually find two relatively large trunks of the nerve which go in and about the sheath of the pulmonary artery, and two large branches to the left bronchus. In addition, on the left four to eight major filaments are present, distributed between the artery and bronchus. No large branches can be seen going to the sheath of the veins. The nerve supply to the artery is less than that to the bronchus but is abundant.

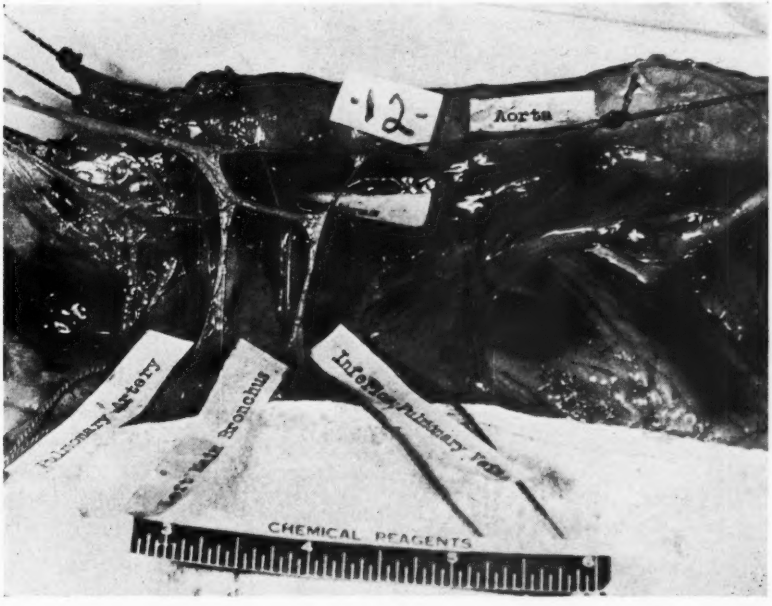

Fig. 1.—Photograph of the distribution of the vagus nerve at the left pulmonary hilum.

On the right side there are usually only two or three main branches and two to four finer filaments. On the right side it appears that the greater portion of the nerve trunks go to the main bronchus, with a meager supply to the artery as compared to the left side.

Fig. 1 demonstrates a dissection of the left hilum with two major and two minor branches going to artery and bronchus. In Fig. 2, the right hilum is shown with six branches to the bronchus and only one branch of significance to the pulmonary artery.

Selection of Patients.—Only patients who have been completely incapacitated from the disease have been selected for surgical intervention. The diversi-

form nature of asthma, vague multiple etiological factors and utter lack of precise knowledge of the physiology of the nerve supply of the lungs leaves only an empirical approach for choosing subjects for operation.

The first patient subjected to operation was a 29-year-old white woman, who had had severe asthma for fifteen years. During the four years before the operation she spent the majority of her time in a hospital.

She was first seen in June, 1947, at which time she was receiving oxygen and helium and her condition was critical. Adrenalin, aminophyllin, Benadryl and, finally, ether in oil and avertin were given with no appreciable effect on the status asthmaticus. Finally, 50 c.c. of ether in 1,000 c.c. of saline (100 mg. per kilogram of body weight) was given. The status was broken and about two weeks later the operation was performed. In this first case in which a left-sided

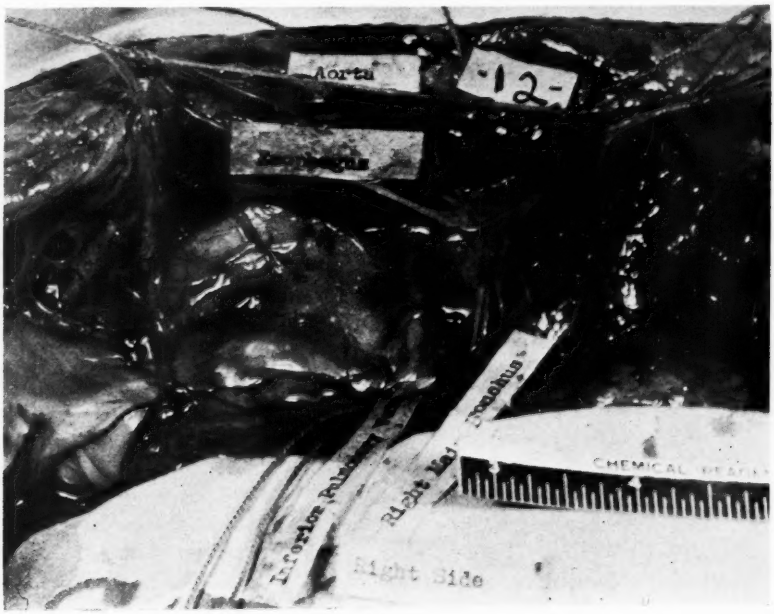

Fig. 2.—Appearance of the vagus nerve at the right pulmonary hilum.

denervation was done, there has been complete relief from the disease for thirty-four months. The left side has been the site of initial operation in all subsequent cases because of the relative abundance of nerve supply. Later attempts to treat severe asthma by surgical intervention were stimulated by this original dramatic result.

It, of course, occurred to us that factors other than the operation might have been responsible for the relief. Accordingly, in 12 cases patients were subjected to avertin-ether anesthesia from one to four hours and allowed to recover from the effects of the anesthetic. In our series, the longest respite from an asthmatic attack was forty-eight hours.

The same precaution was taken concerning the effects of bronchoscopy on the asthmatic patient and again relief for more than a few days was not obtained.

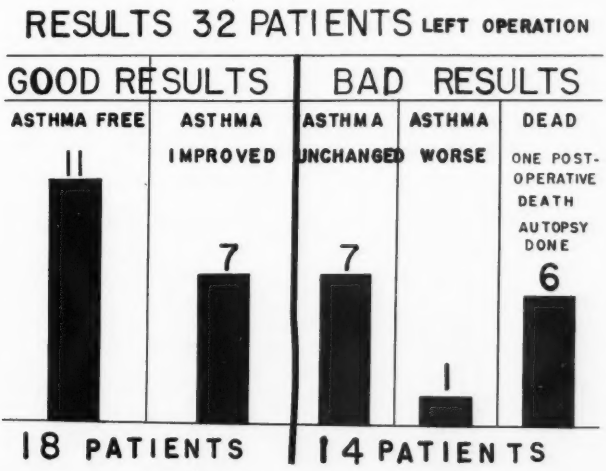

Fig. 3.—The results in 32 patients subjected to left pulmonary denervation.

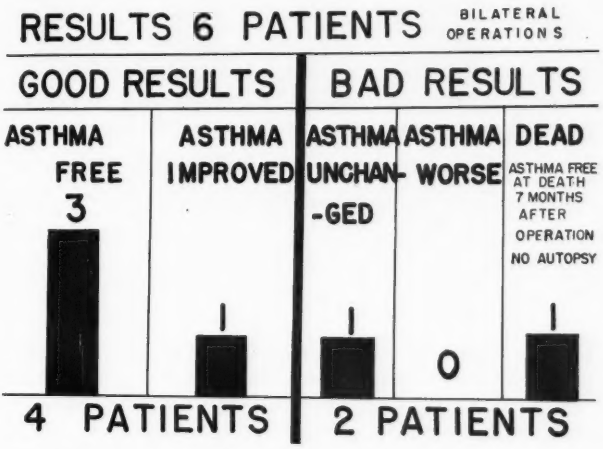

Fig. 4.—The results in six patients treated by bilateral pulmonary denervation.

Several methods have been employed in an attempt to find an objective test to estimate whether or not operative interference would be beneficial. Reactions to injections of adrenalin, aminophyllin, and other drugs have not, in our series, been useful in the selection of patients. In this connection it is important to record that more than 50 per cent of the cases were "adrenalin fast."

Studies of lung volume, including determinations of residual air, have offered no help in the selection of patients, but have been useful in evaluating the postoperative results. Attempts to obtain bronchospirometric readings have been abandoned because the patients have been so short of breath reliable data could not be obtained.

Results.—The results in 32 patients subjected to left-sided denervation are shown in Fig. 3. Of the 32 cases, 11 are free of asthma; 7 patients believe they are definitely improved; and in 7 the disease is unchanged. In 1 the asthma is worse. The categories of improved and worse, in our opinion, have little significance.

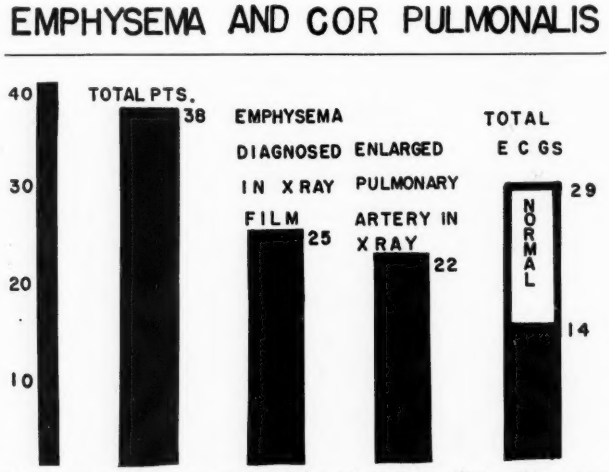

Fig. 5.—Incidence of emphysema and cor pulmonale in 38 patients with severe asthma.

In the entire series of 38 cases, there has been one operative death. This was in a man 73 years of age, who had suffered from severe asthma for many years and had far-advanced emphysema and cor pulmonale. He was in the hospital for some time and we were persuaded to undertake the operation because he had threatened to commit suicide if something was not tried in his case. The operation was tolerated well, but on the second postoperative day, while sitting in a chair having breakfast, he died suddenly. The post-mortem examination revealed a spontaneous pneumothorax on the right side; the left side had been operated upon. The remaining six deaths occurred at intervals from six to eighteen months following surgical intervention. The late mortality in this group of cases is not surprising when one considers the incidence of cor pulmonale and advanced emphysema in these patients.

The results in patients subjected to bilateral denervation are shown in Fig. 4. Three patients are free of asthma, one considers himself greatly improved and the disease is unchanged in one. The one death in this group was in a patient who was free of asthma for seven months after operation. He had cor pulmonale and severe emphysema and was found dead at home by his family. Permission for post-mortem examination could not be obtained.

Emphysema and Cor Pulmonale.—Fig. 5 demonstrates the incidence of emphysema and cor pulmonale in the group. A clinical impression of emphysema was not accepted and only in those patients in whom emphysema was obvious on roentgen examination was the diagnosis recorded. Cases included in the column labeled enlarged pulmonary arteries are those in which an unequivocal diagnosis of cor pulmonale could be made. These data make obvious the reasons for the late mortality in the group.

It is interesting and somewhat bewildering that relief of symptoms was effected in patients with emphysema in about the same proportion as in those without this complication.

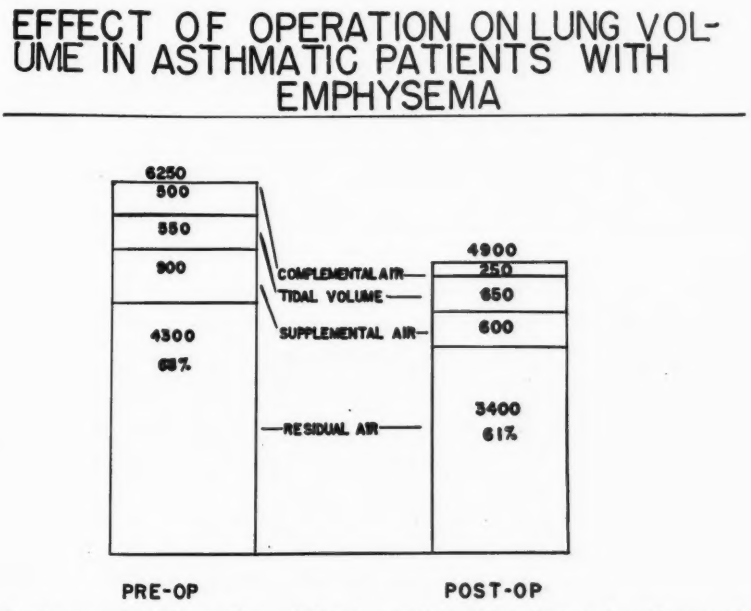

Fig. 6.—An example of lung volume studies in a patient with asthma and emphysema, before and after operation.

Lung Volume Studies.—Fifteen patients have been studied before and after operation with measurements of total lung volumes and the percentage of residual air, utilizing a helium spirometer modeled after the McMichael modification of the Christie method. A Sanborn spirometer and a helium-air analyzer manufactured by the Cambridge Company have been employed. Fig. 6 reveals the apparent effects of the operation on lung volume in a patient with severe asthma and emphysema. The interval between the preoperative and postoperative studies was eleven days. Temporary reduction in vital capacity is expected after any intrathoracic operation. Longer periods of observation and a larger series of patients will be required before definite conclusions on the effects on lung volumes can be accepted.

Pulmonary Artery Pressures.—Pulmonary artery pressure readings before and after operations in human subjects have been hampered by technical difficulties but will be accomplished in the future. The importance of these studies is suggested by observations made on dogs which have had bilateral

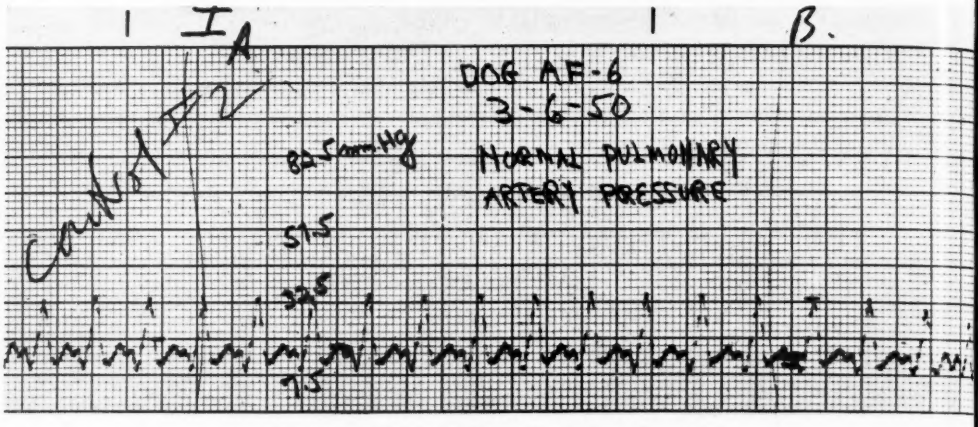

Fig. 7.—Pulmonary artery pressures in a normal dog.

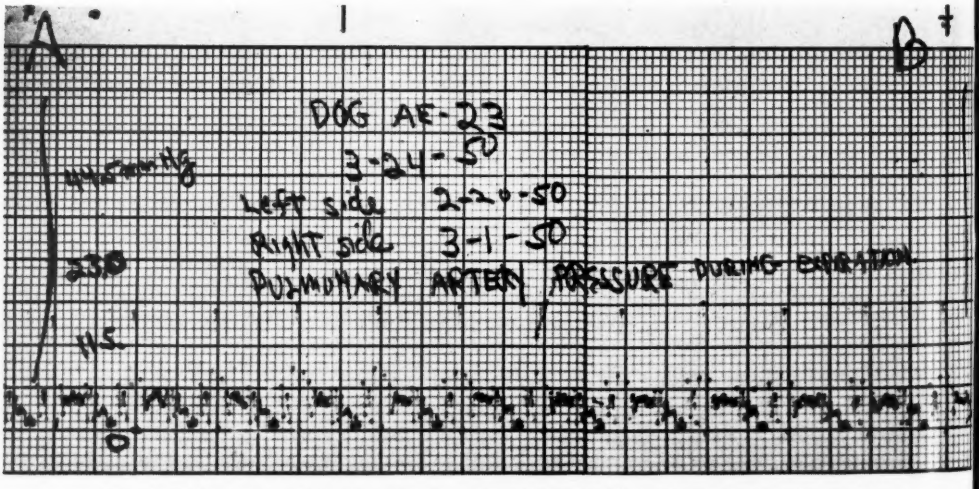

Fig. 8.—Pulmonary artery pressures in a dog following bilateral pulmonary denervation.

pulmonary denervations. Control animals were subjected to bilateral thoracotomies without interference to the nerve supply. The other series of dogs had bilateral denervations comparable to the operation which has been performed in the human being. Fig. 7 reveals normal pulmonary artery pressure readings in a control dog, of 32 mm. of mercury systolic pressure and 10 mm. of mercury

diastolic. Fig. 8 demonstrates the pressure tracing on a dog subjected to bilateral pulmonary denervation. The pressures in this animal were 17 mm. of mercury systolic and 3 mm. of mercury diastolic. These changes in pressure are to be confirmed in the human being but the findings are suggestive.

Ramifications of attempts to study the functions of the vagus nerves include observations on tolerance to lycopodium spore injections in normal and denervated animals and observations on electrocardiographic tracings in both human beings and animals with extensive vagus nerve destruction. These will be reported in separate communications.

SUMMARY

A total of 38 patients have undergone surgical intervention for the treatment of intractable asthma. In 14 cases the patients are free of disease. Eight patients consider themselves improved. In 8 cases the disease is unchanged; and in one instance the asthma appears to be worse. There was one postoperative death and six late deaths.

These data demonstrate the bewildering consequences of an empirical surgical approach.

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DISCUSSION ON "A PHYSIOLOGIC EVALUATION OF VAGUS SECTION FOR BRONCHIAL ASTHMA" BY DR. KARL P. KLASSEN, DR. DOUGLAS R. MORTON, AND DR. GEORGE M. CURTIS;* "THERAPEUTIC STATUS OF PULMONARY AUTONOMIC NERVE SURGERY" BY DR. OSLER A. ABBOTT, DR. WILLIAM A. HOPKINS, AND DR. PAUL H. GUILFOIL;† AND "THE SURGICAL TREATMENT OF INTRACTABLE ASTHMA" BY DR. BRIAN BLADES, DR. EDWARD J. BEATTIE, JR., AND DR. WILLIAM S. ELIAS

DR. A. J. GRACE, London, Ontario.—This problem interested me first in 1945, and at the St. Louis meeting when Dr. Carr presented his paper on autonomic work along this line, I presented a brief survey of 11 cases, a very small series, which had been done in the preceding 15 months. Actually, that discussion did not find its way into the JOURNAL, for some reason, and I thought it might be worth while to bring up the clinical survey of those cases to date and to put that material in tabulated form. I am omitting further cases done more recently. There are a few; I have limited them strictly because of the

*See page 552 for article by Klassen, Morton, and Curtis.
†See page 571 for article by Abbott, Hopkins, and Guilfoil.

FOLLOW-UP RESULTS: BILATERAL PULMONARY VAGAL DENERVATION FOR INTRACTABLE ASTHMA

PATIENT	AGE (YEARS)	SEX	DURATION DISEASE (YEARS)	OPERATIVE YEAR	RESULTS		DEAD
					EARLY	LATE	
A. I.	37	M	3	1946	Good	Good	—
R. J.	27	M	8	1946	Good	Good	—
M. R.	31	M	25	1946	Good	Good	—
H. S.	55	M	28	1946	Doubtful	Fair	—
E. W.	56	M	26	1946	Fair	Fair	—
F. S.	70	M	16	1946	Good	—	4 months
D. P.	24	M	15	1945	Fair	Poor	2 years
F. T.	35	F	10	1946	Fair	Poor	—
E. B.	44	M	7	1946	Poor	Poor	—
F. R.	50	M	27	1946	Poor	Poor	—
E. S.	51	F	3	1947	Poor	Poor	1½ years

confused state of our thinking and understanding of the basic physiology involved, and have felt that we should be forced into this procedure only for absolutely hopeless cases of the type described by Dr. Blades and our other associates.

This slide tabulates the essential data on 11 cases completed between November, 1945, and February, 1947, giving a follow-up period exceeding three years in all patients. The age and sex of each patient are listed along with the duration of disabling asthma The operation was a fairly radical type of resection of every demonstrable vagal connection on both sides, done in two stages. An attempt has been made to evaluate the status of each individual in relation to the passage of time. I wish to emphasize the fact that some patients failed to maintain initial improvement, while one patient in particular seemed to gain steadily with the passing years, after a disappointing immediate response. In general, I am not happy about the results in the older age groups, although the man 70 years of age seemed most successful until his early death on a cardiac basis.

In this very limited series the only striking results were shown by the first three, relatively young men; each of these has been restored sufficiently to hold down a full-time job satisfactorily, something which was absolutely impossible before operation. These cases encourage one, but I am not at all sure that even they are in any sense "cured" of their asthma. They are free from any gross disability.

As stressed by Dr. Blades and others, we must be very careful in assessing "results" after any operative procedure for asthma. The time factor must receive consideration along with many other variables. The entire problem calls for much more investigation.

DR. ROBERT P. GLOVER, Philadelphia.—Our results with complete denervation of the lung, at least our understanding of complete denervation of the lung, carried over a two-year period, are summarized on the first slide. Our operative approach is to remove or resect segments of all the branches of the vagus nerve on the left side and the right side, from the recurrent laryngeal nerve down. We do not transect the main trunk of the vagus nerve. We also carry out a circumcisional denudation of an area about one inch along the course of the bronchus, the pulmonary artery and the pulmonary veins, and remove or detach the inferior pulmonary ligament. This has been carried on for a period of two years.

We were stimulated in this work by the work of Carr and of Blades. We have carried out a unilateral procedure on the left side in 25 cases and a bilateral procedure in 4 cases. Five of these patients are now asymptomatic; 6 others we consider to be improved; their trouble at present is concerned with secretions and not with asthma per se. There are 18 unimproved cases, including four deaths; two of the latter were operative, two have since died in what appeared to be status asthmaticus. Two of the unimproved cases had the major bronchus completely transected and then repaired; it did not seem to improve the result. Four other cases had removal of the sympathetic ganglia from the second to the

fifth thoracic vertebrae also without improvement; one of these was bilateral. All these cases have been followed to date. As a matter of fact, we are having difficulty in some instances in losing the patients, particularly those who are still having trouble. Sections removed from the lung in one-half the cases have been examined pathologically, and in only one was there evidence of emphysema.

DR. LAWRENCE MISCALL, New York.—In 1942, we reported 21 cases upon which we had done some form of sympathectomy for intractable asthma. These were patients who crowded the Bellevue Clinic. They had run through the gamut of all medical care but they were there daily. We tried to select patients for surgery in this way: the medical service had turned them over as being unaided by anything they could offer. We took patients who had not been treated for an extended period of time in the allergy clinic; most had been labeled as intractable asthma on a recurrent infectional basis. We were prompted to attack from the sympathetic side rather than posterior pulmonary plexus resection because of the experience of Rienhoff. We selected patients for operation only after they had been benefited by a stellate block. Of 61 patients whom we blocked we were able to obtain variable relief in 47, or 78 per cent. Of this group we accepted 21 patients for operation because of a definite improvement after block, which was not maintained. In 1942, we had followed them for from two months to two years. We were greatly impressed with the group. We thought we had the method by which we could select those who would be benefited by operation for a long period of time.

The war came along and the work was suspended. Since the war we have been able to follow 11 of these patients; 6 have had good results; the others have had miserable failures, which is about a 50 per cent failure rate. Since that time we have been doing a much more widespread operation; resection, bilaterally, of the upper dorsal chain and a parasympathetic denervation. Our results are still no better. We can obtain only about 50 per cent cures. I think this depends upon what one considers a cure. The only ones we have accepted are patients who do not come back to the Clinic routinely. I think the solution of the asthma problem is going to come when we are able to define a disease and not be treating a symptom complex.

DR. RALPH ADAMS, Woodbury, Tenn.—One may further confound confusion by a report on 21 patients, the last one operated on more than a year ago, all of whom at this time have proved to be failures. Some of these cases were reported following Dr. Carr's report; some of those, as some of the cases reported this morning, were brilliant early successes and led us to perform further operations upon additional patients. The problem at this time seems to me to be similar to that of removal of the thymus gland for myasthenia gravis uncomplicated by tumor; follow them long enough and they will again have myasthenia gravis; as the asthmatics will again have asthma.

In the section of the country where I live, financial considerations are of greater importance than in some sections where I have lived. It was of interest to determine the cost to the patient in a group of eight of these denervations for asthma. The cost of hospitalization, for these patients having bilateral combined extensive sympathetic and parasympathetic denervations, as I understand it, was slightly over $500 per patient. In the end, these patients, if they are still alive without having died from a recurrent attack of status asthmaticus, have had no more than a term of symptomatic improvement from operation. That amount of money will buy a great deal of aminophyllin or adrenalin.

DR. DUANE CARR, Memphis, Tenn.—I, too, am from the low income section of the country. From the excellent presentations that have been given, it becomes apparent that a certain number of patients with previously intractable asthma are definitely benefited by any one of the various surgical attacks upon the autonomic nervous system. But the wide variation in results obtained indicates that none of the procedures strikes at the root of the trouble.

It so happens that we favor the dorsal sympathetic ganglionectomy because it is so cheap; at least it involves less surgery than the more radical transpleural operations and is therefore better tolerated by some of these extremely ill patients, and we believe this operation gets away from the postoperative pulmonary function restrictions which do occur following a transpleural operation. The results obtained are not materially different from those reported following more radical procedures.

I believe it becomes apparent to everyone that there must be in asthma some basic, fundamental, underlying disease of the autonomic nervous system. Asthma is but one manifestation of it, and is perhaps closely related to other degenerative diseases such as hypertension. It has been a common finding that in each ganglion removed for the treatment of asthma degenerative change has been found. This is not only our observation but that of others.

In addition, we must know something more about the modus operandi of asthma. It has not been proved by anyone that bronchial spasm actually exists; a simple demonstration of diminution of bronchial caliber does not necessarily mean bronchial spasm. There is not one whit of evidence to show that bronchial muscles contract to throw the patient into an asthmatic attack, any more than there is to indicate that the nasal bones contract when one has an attack of hay fever. We do know that changes in the bronchial mucous membranes occur as a result of numerous stimuli, such as direct contact with allergens, changes in temperature, emotion, infection, and a host of others which do *not* produce asthma in a *normal individual.*

We are impressed with the way asthma disappears in the youngster as he reaches the age of puberty, and the improvement in asthma as a result of the demand stimuli of an operation. It occurs to us that a fruitful field of investigation is the determination of the pathologic changes occurring in the autonomic nervous system in asthma, and in its governing hormone producing organs. Every patient dying of status asthmaticus, or who has been a chronic asthmatic, should at autopsy have a meticulous microscopic examination of the autonomic nerves and ganglia, and of the hypophysis and adrenal cortex at least. Until we learn what the basic pathologic and pathophysiologic action in asthma is, our treatment by attacks on the autonomic nervous system will be empirical, and all medical treatment will be no more than symptomatic.

DR. H. J. STANFORD, Tucson.—I should like to add to the comments of Dr. Adams and Dr. Carr, that perhaps our approach to the treatment of bronchial asthma is not exactly in the right direction. My own early enthusiasm following some highly satisfactory results has been dampened by later failures. This does not mean that we should discard surgical treatment. However, I can best illustrate the need for further study by giving the case history of one patient.

This man was first treated for involutional melancholia back east and received electric shock therapy. He improved and went back to work as a factory executive. One year later he developed intractable bronchial asthma and went through the gamut of treatment for this condition. He had severe asthma for the next five years, requiring repeated hospitalization. About six months ago, I found on bronchoscopy that he had marked bilateral bronchial spasm and blockage of the bronchi with inspissated mucus and bronchial casts. Following this, I did a right-sided pulmonary denervation that included the sympathetic chain down to the sixth thoracic, the posterior pulmonary plexus, and stripping the pulmonary artery.

During the first three postoperative days there was no improvement. From the fourth day on he had complete cessation of his asthma which lasted for five weeks. After this his asthma returned and, in addition, he went into a manic psychosis state. The psychiatric consultant called in advised shock therapy. He was flown back east, where he received a series of electric shock treatments with no improvement. He was next given a course of ACTH therapy for ten days. This was more than two months ago. He had an immediate remarkable cessation of all his symptoms, is back at work, and has

had no asthmatic attacks to date. The result of the therapy with ACTH is what I wish to emphasize, because it points to a possible new approach to the entire problem of cause and treatment of bronchial asthma.

DR. J. H. WALKER, Boston.—We have been doing surgery at the Overholt Thoracic Clinic for bronchial asthma for two years. We have studied this group of patients through sympathetic blocks and bronchography, and it has been most interesting to us to find that 40 per cent of our 25 patients have had some type of abnormal localized pathology that has needed resection. Thirty-five per cent of our patients have responded to sympathetic block and have had sympathetic surgery. We have noted improvement in about two-thirds of these. Three of these patients had only one lung, one was congenital and two from pneumonectomy eight to ten years ago; two of these patients have had dramatic results.

It is interesting that none of the cases treated with sympathectomy, or that responded to a block, have had any localized pulmonary pathology. Cases that we have treated by pulmonary neurectomy and excision of diseased pulmonary tissue have given the best results. We have noted improvement in about 75 per cent of them, and it has been a most satisfactory type of improvement. I want to repeat, that his has been done only for a period of two years.

DR. EMILE HOLMAN, San Francisco.—We are indeed indebted to these various authors for bringing us up to date on the surgical efforts to cure this intractable disease. I am wondering, however, if we are not on the verge of a new era in treatment of this disease, as suggested by one of the preceding speakers. A member of our faculty has for thirteen years injected himself every two to three hours, night and day, with epinephrine for bronchial asthma. In periods of stress, as during a lecture, he has injected himself as often as every thirty minutes. On March 7, 1950, he entered the hospital in a state of severe asthma; intravenous aminophyllin failed, and epinephrine no longer produced the same effects as formerly. He had marked pulmonary edema. On March 7, he received 100 mg. of Cortisone intramuscularly; on March 10, he said he felt better than he had in five years, and gleefully reported that he had injected himself only four times in the preceding night. The Cortisone was dropped on March 13, to 33 mg., and he is now on a daily maintenance dose of 25 mg. of Cortisone, and is completely free of asthma.

DR. GEORGE M. CURTIS, Columbus, Ohio.—Our studies have been made in an attempt to find something helpful concerning the clinical physiology of the human tracheobronchial tree. And, consequently, intractable asthma, widely thought to be a manifestation of smooth muscle spasm, has become a part of our observation.

Five features of the neurophysiology of the human bronchi have come under this consideration; the *first*, the sensory nerve supply of the tracheobronchial tree. This has been fairly well worked out from the standpoint of the anatomist; however, it needs better clinical application. It has become apparent that pain of tracheobronchial origin is carried to the central nervous system largely through the vagus. The cough reflex is initiated and the resultant impulses are carried to the central nervous system mainly by means of the vagus. Those are our two most useful clinical findings thus far.

The *second* has to do with the motor activity of the smooth muscle in the tracheobronchial tree. There is a definite band between the ends of the horseshoe formed by the tracheal rings. There are definite sheaths around the bronchioles. It is difficult to dissociate smooth muscle from the clinical picture of intractable asthma, even if we consider, as Dr. Holman has suggested, the existence of a hormonal mechanism. The motor control of this smooth muscle appears to an extent through the vagus. In fact, the vagus has been termed the "pulmonary motor nerve." On the other hand, our studies on bronchial asthma appear to show that after bilateral vagus section there remains spasm of the bronchial smooth muscle.

Our *third* approach has concerned the secretory activity of the bronchi and of the trachea. There are two types of secretion: the first, from the goblet cells in the epithelium;

the second, from the bronchial glands, which are mixed glands and therefore may at times form a thick, more mucoid secretion; or at other times, a more watery fluid. The nerve control of bronchial secretion thus becomes important. It is questionable, however, how much nerve control exists over the goblet cell.

Our *fourth* point has to do with ciliary activity. This is of considerable significance. Thus, in the discussion this morning we heard that if high vagotomy is done the patient may develop a wet lung. One might think that this could be due to inadequacy of the cilia. Ciliary movement is one of the oldest forms of movement, next to amoeboid. There is no apparent connection between the nervous system and ciliary activity.

The *fifth* factor has to do with the causation of edema of the bronchial mucosa. Edema may be precipitated by psychosomatic factors. Therefore there is possible an effect from the central nervous system.

We have approached the problem through these five avenues, from the standpoint of useful clinical physiology. However, thus far we have not the solution of intractable asthma, since we feel the same as others who have expressed themselves this morning.

DR. E. A. GAENSLER, Mattapan, Mass.—Objective physiologic evaluation of patients with bronchial asthma before and after surgery for its relief are of the utmost importance. Only results of such laboratory studies will eventually show various surgical procedures in their proper light. In conjunction with a preoperative medical and psychiatric evaluation, such physiologic studies should be expected to do three things: (1) aid in ruling out a number of patients whose respiratory difficulty is due to causes other than bronchial asthma; (2) give an early indication between and after surgical stages of the results of such surgery; and (3) formulate a set of physiologic findings and responses which, after some experience, will aid in the preoperative prediction of the likelihood of success of surgery.

A number of interesting and valuable objective observations for the study of asthma have been described this morning. We presume to add a number of suggestions derived from our experience in the study of more than 120 patients with varying degrees of bronchial asthma and pulmonary emphysema, only because the number of patients with asthma of sufficient severity to warrant surgery is at the present time small, and we feel that an earlier and better evaluation of such surgery will be possible if more and better tests before and after surgery are used for the evaluation of results.

Vital capacity determinations are not only unreliable in the presence of bronchospasm and/or loss of pulmonary elasticity, but also give a false impression of the degree of pulmonary insufficiency present. The maximum breathing capacity is the single most valuable test except in those patients where attacks of asthma are elicited by this test. Studies of patients with bronchial asthma could not be carried out on one or two occasions, but patients should come to the laboratory at scheduled repeated time intervals, and identical tests should be repeated at weekly or biweekly intervals for at least four to eight weeks, in order to give the patient an opportunity to become acquainted with the laboratory staff and the testing devices. Only such repeated studies can possibly lead to a relatively good base line in asthmatic patients where functional results often vary a great deal more with home and business conditions than with medical or surgical therapy. Tests should be repeated not only after the administration of bronchodilator substances but also after artificial induction of asthma by intravenous injection of histamine and methacholine, as outlined by Curry and Lowell and Segal and Beakey. Preoperative responses to one or the other drug may eventually give a clue as to good prospective surgical candidates. Bronchospirometry before, between, and after surgical stages has been found of great value, particularly if asthmatic attacks are induced as outlined above, during the course of the procedure. Finally, pneumatographic studies between and during attacks aid in the measurement of inspiratory-expiratory time ratios and air flow velocities.

A small number of patients studied by us in this manner during and after surgery have all had bilateral vagectomy below the recurrent laryngeal nerve, and posterior pulmonary plexus resections—operations carried out by Dr. John W. Strieder and Dr. Dwight E. Harken.

No conclusions can be drawn at this time, but three observations may be recorded here. Unilateral operations have been found to be of no value. Patients with advanced pulmonary emphysema, secondary to long-standing bronchial asthma as evidenced by poor bronchodilator and bronchoconstrictor response, persistently large residual air values and persistent low arterial oxygen tensions and high carbon dioxide tensions after exercise, have not benefited by such surgery. Interruption of the innervation of the lungs cannot be expected to repair lungs with permanent and irreversible anatomic destruction and disruption. And, last, there is good evidence obtained during bronchospirometry with artificially induced asthma, that occasional patients have predominantly unilateral asthma in the absence of unilateral anatomic disease.

DR. MORTON (Closing).—This discussion has been quite prolonged, so I merely wish to thank the men who have participated.

DR. ABBOTT (closing).—The lack of satisfactory results in the presence of diffuse suppurative disease or in cases with nonresectable amounts of pulmonary destruction should be stressed. I suspect that after a certain duration of disease, results from complete plexectomy are less satisfactary. The loss of ciliary function in long-standing bronchial asthma is well known. We feel that with proper selection of patients, pulmonary denervation will find its proper place in the treatment of bronchial asthma.

DR. BLADES (closing).—It seems to me the principal accomplishment of this morning's discussion has been to stimulate interest in the surgical treatment of asthma.

The costs of hospitalization in Tennessee are amazing. In my opinion, a $500 purchase of adrenalin for the adrenalin-fast patient is as poor an investment as $500 spent for hospitalization without good results.

The presence or absence of bronchial constriction cannot, in my opinion, be determined accurately either by bronchograms or bronchoscopic examinations. Dr. Holman's comments on the use of Cortisone in the treatment of asthma are interesting. The availability of this drug may change the whole problem in the treatment of asthma and make surgical intervention completely undesirable.

The psychogenic factor in asthma has been mentioned. This is well known, and perhaps if these patients were subjected to prefrontal lobotomy they might still have asthma but would not care. This important aspect of the disease is one of the many imponderables of the question.

THE EXPERIMENTAL USE OF HOMOGENOUS TRACHEAL TRANSPLANTS IN THE RESTORATION OF CONTINUITY OF THE TRACHEOBRONCHIAL TREE

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DETROIT, MICH.

INTRODUCTION

THE rapid advances in surgery of the thoracic viscera which have occurred during these last twenty-five years have made healing and regeneration of tissue within the tracheobronchial tree of significant practical importance. Taffel,[1] in 1940, reported the use of fascia in the repair of small tracheal defects in dogs. Daniel,[2] in 1948, reported experiments in which rigid tubes were used to bridge defects in the trachea and the primary bronchi. He discussed in detail the growth of the tracheobronchial wall in relation to these rigid tubes. Hanlon,[3] in 1948, reported his observations in dogs, where gelatin sponge was used in the closure of defects of the bronchus. Jackson and associates[4] published experiments in 1949 observing the results of end-to-end anastomosis of the bronchi following resections of segments of the primary bronchus. They found this could be performed successfully in dogs without significant morbidity to the lung or bronchus either functionally or anatomically and described a technique in detail.

However, the problem posed in the bridging of extensive defects of the trachea and bronchus where end-to-end anastomosis is not feasible presents a stimulating challenge. Ideally one must construct a tube in the tracheobronchial system that will remain at least semirigid, and will become an integral part of that system permanently allowing for the passage of air and secretions. Should one pursue successfully this endeavor, then the discouraging problem of extensive destructive lesions of the trachea and possibly tracheobronchial segments, would lend itself to surgical treatment.

One of us (E. J. O'B.) became intensely interested in this subject after reviewing the recent work of Gebauer. The latter[5] published work in 1949 in which plastic repair of bronchial stenoses was accomplished by using skin grafts which were held rigid by the interlacing of wire sutures. After discussions with Gebauer, we were led to attempt experiments to restore the tracheal continuity using living and preserved tracheal grafts.

HISTORICAL REVIEW OF TRANSPLANTATION

The study of tissue transplantation is not new to this decade. Anatomists and physiologists have long maintained such an interest and speculated on its practical possi-

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bilities. Probably one of the first experiments to be performed on the grafting of cutaneous tissue, can be found in the writings of John Hunter (1794) and is here related in his own words.

"I took the spur from the leg of a young cock, and placed it in the situation of the spur in the leg of a hen chicken; it took root, the chicken grew to a hen, but at first no spur grew, while the spur that was left on the other leg of the cock grew as usual. This experiment I have repeated several times in the same summer, with the same effects, which led me to conceive that the spur of a cock would not grow upon a hen and that they were, therefore, to be considered as distinct animals, having, very distinct powers. In order to ascertain this, I took the spurs of hen chickens and placed them on the legs of young cocks. I found that those that took root grew nearly as fast and to as large a size as the natural spur on the other leg."[6]

Hunter was also a strong advocate of transplantation of teeth from one person to another. This, a prevalent practice in his day, soon fell into disrepute. To quote Hunter:

"The scion tooth, or that which is to be transplanted, should be a full grown young tooth; young, because the principle of life and union is much stronger in such than in old ones. . . . The new teeth should always be perfectly sound, and taken from a mouth which has the appearance of that of a person sound and healthy."[7]

Time has shown that his views on the viability of grafted teeth were largely erroneous (Colyer,[8] 1913). His work is of great historical interest and demonstrates the tremendous scientific vitality with which he was gifted.

It is of note, that in Hunter's time, in Europe as well as America, high prices were offered for teeth for transplantation. Taylor,[9] in his *History of Dentistry,* noted a newspaper advertisement in 1782 offering four guineas for each sound front tooth. A dentist by the name of Jullion charged a fee of five guineas for transplanting a live tooth and two guineas for dead ones. One also remembers the account of the girl Fantine in *Les Miserables,* who offers the sale of her teeth to provide money for the care of her child.

In the development of tissue transplanting, the use of skin has always been of major interest. In this paper we are only concerned with the problem of the transplanting of tissue from one individual to another of the same species. To date it can be stated that the success of homogenous transplants of skin is unsettled, questionable, and opinions are widely divergent. Early workers claimed success. Such is expressed by Oshima[11] in 1914. Lexer,[12] in 1911, had no success at all. Masson,[13] in 1918; Dyke,[14] in 1922, believed that the success of homoio-skin grafts depended on blood compatability of donor and recipient.

Dobrzaniecki,[15] in 1929, thought that except between uniovular twins, such grafts are never permanently successful, though survival is prolonged by identical blood grouping. Trusler and Cogswell,[16] in 1935, believed that though such grafts may at first adhere well and appear to have taken, they always slough later.

Willis,[10] in 1939, delivering the Victorian Lecture (University of Melbourne), presented a comprehensive review of tissue transplantation and its relationship to surgery. His summary of homeotransplantation included numerous tissue types, embryonic as well as adult. He felt that generally in all homeotransplantations, there was not a permanent growth of the graft, as such. Says he of bone: "to me the evidence suggests that, on the one hand the greater bulk of a large bone graft (homogenous) dies and is replaced, but in suitably small fragments parts survive and contribute to osteogenic repair."

Attempts to treat Addison's disease by transplantation of adrenal tissue from other people or fresh corpses have been reported with temporary benefit. Hurst,[17] in 1922, Pybus,[18] in 1924, and Beer,[19] in 1934 reported such cases.

Other reports are found in reference to transplantation of ovary, testes, and pancreas, but no proved permanent result is maintained. A group of German scientists became intensely interested in the problem in the decade 1920 to 1930 and made numerous investigations. Gins,[20] in 1927, discussed the failure of epithelial cells to survive in transplanted

tissue. His observations were concerned with the lack of stimulus to growth and the autolysis due to formation of lysing tissue juices. Baetzner and Beck[21] discussed the problem of "homeotransplantation" in 1928, and reported the failure of these tissues to retain their individuality in the host. Similar studies were published by Fischer[23] in 1929. Bruda,[22] in 1930, attempted to show the relationship between the success of homeoplastic grafting and the reticulo-endothelial system. Ruditskiy,[24] in 1936, conducted similar investigations.

The important biochemical factors preventing growth of grafts was discussed by Loeb and Addison[25] in 1909. This effect was felt to be less in autogenous and strongest in heterogenous transplanting. They felt the tissue fluids of the host have a harmful effect on the transplanted structure. The closer the relationship to the host tissue, the more chance the cells have to live. Loeb declared that dissimilarity between two tissues leads to the development of heterotoxins which are directly responsible for the reaction on the part of connective tissue and lymphocytes in the host tissue, as well as interference with vascularization.

Loeb,[26] in 1908, from experimental work concluded that there exists a difference between the adequacy of the different species as a soil for epithelium, and that the more nearly related two species are, the better will be the growth of epithelium.

Most of these factors are eliminated with the use of preserved transplants however, since the cells are not viable. One must depend on the growth of connective tissue, epithelium, and other forms, from the surrounding host tissue. Weiner,[27] in 1943, discussed the use of preserved grafts and transplanted the conjunctiva of the cow to the eye of the rabbit with some success. His transplants were formalinized.

Greene,[28] in 1943, found that embryonic mammalian tissues could be grown in adult alien species and that such transfer was readily effected as homologous embryonic transfer. Willis,[10] in his report, found embryonic tissue more adaptable. Greene,[29] in 1945, reported the production of carcinoma and sarcoma in transplanted embryonic tissue treated with methylcholanthrene. He postulated that the reserve stem or partially differentiated cells of the body formed the source of neoplastic cells in adult animals.

Sheehan,[30] in 1943, discussed various types of tissue grafting and advised the removal of the perichondrium from autogenous and homogenous cartilage grafts. He felt this essential to the success of the grafting.

Algeri,[31] in 1945, ingeniously using transparent chambers inserted in skin flaps in mice, described the vascular reaction to tissue transplants. He reported the early accumulation of fluid and leucocytes followed by a rapid and dense vascularization, thence by scar tissue growth. In tumor transplants he declared the outstanding characteristic of the neoplastic cell to be its capacity to elicit continued growth of new capillary endothelium from the host which was sharply different from the reaction to normal tissue and an expression of neoplastic change.

With regard to the clinical use of autogenous transplants, Neuhoff[32] reported in 1941 the successful use of a fat mass removed from above the iliac crest to close a pulmonary cavity with bronchial fistula.

Harrison,[33] in 1936, reported a case of tracheal stricture following attempted suicide. He removed the stricture and placed a Thiersch skin graft over the raw surface. A successful recovery followed.

Negus,[34] in 1938, reported the use of thin autogenous skin grafts over the vocal cords to prevent their adherence after surgical separation. He also used skin flaps to reconstruct the continuity of the laryngotracheal segment in cases of fistula following irradiation.

Swinburne,[35] in 1941, discussed in detail the problem of laryngotracheal stenosis and the successful use of thin skin grafts in their plastic repair.

Nach,[36] in 1943, discussing methods in the closure of tracheal defects, made reference to the use of free fascia. He described the new tracheal wall following this grafting as composed of:

1. A layer of pseudostratified epithelium.
2. A layer of submucosa with occasional mucous glands, a few small islands of new cartilage, but with occasional exceptions, no fibers of muscularis mucosa.
3. An outer layer of supporting adult connective tissue.

From this summary one can say with few exceptions, that adult homogeneous grafts give no permanent structure in tissue grafting. There is some indication that embryonic tissue may be more successful. Fresh homeotransplants meet a great resistance in the host, with resultant liquefaction. This is principally due to the biochemical reactions set up in the host. Preserved grafts are not viable and do not excite so severe a reaction. When transplanted, they act as a superstructure, are absorbed, and in the case of the trachea, the end result of the tissue wall may be as described by Nach[36] (three layers as described in the preceding paragraph).

Fig. 1.—Massive liquefaction and death in 10 days with use of a fresh, viable, homogenous transplant.

It was desired by the authors to explore the possibilities experimentally, of bridging varying lengths of produced defects in the tracheobronchial tree of dogs, making use of homogenous tracheal transplants. The experiments were divided into two groups for evaluation and study.

Group 1.—Repair of small defects in the trachea and bronchus using homogenous transplants.

Group 2.—Resection of complete segments of the trachea up to two inches in length and closure with homogenous transplants.

METHODS

Eighteen dogs of nonspecific pedigree were used. Numerous others were used in standardizing the procedures and in setting up the program for study. Surgical procedures were performed under intravenous Nembutal anesthesia. For the cases in which the pleural cavity was entered (gaining access to the bronchus) oxygen was given by intermittent insufflation, making use of an endotracheal tube.

Preparation of the Transplants.—Early in the experiments several dogs were used to test and to standardize the type of transplant to be used. Two dogs of approximately the

same weight were simultaneously anesthetized and complete one-inch segments removed from the trachea through a midline neck incision. The tracheal segments removed were transplanted from one dog to the other, using a simple end-to-end anastomosis of 0000 silk. The tracheobronchial tree was aspirated and the dogs given 100,000 units of penicillin daily. For the first four days, the postoperative course was not unusual. The animals walked out into the runway and ate regularly. However, they then began to stop eating and began to cough. Within ten days they presented signs of definite tracheal obstruction; they were weak, ill, and died rapidly. Fig. 1 presents the autopsy appearance of such a specimen. Gross section presented the picture of severe edema and liquefaction of the transplant with complete collapse of that portion of the trachea. Microscopic section as shown in Fig. 2, revealed edema, autolysis of tissue, with little evidence of viability or of ingrowth of connective tissue.

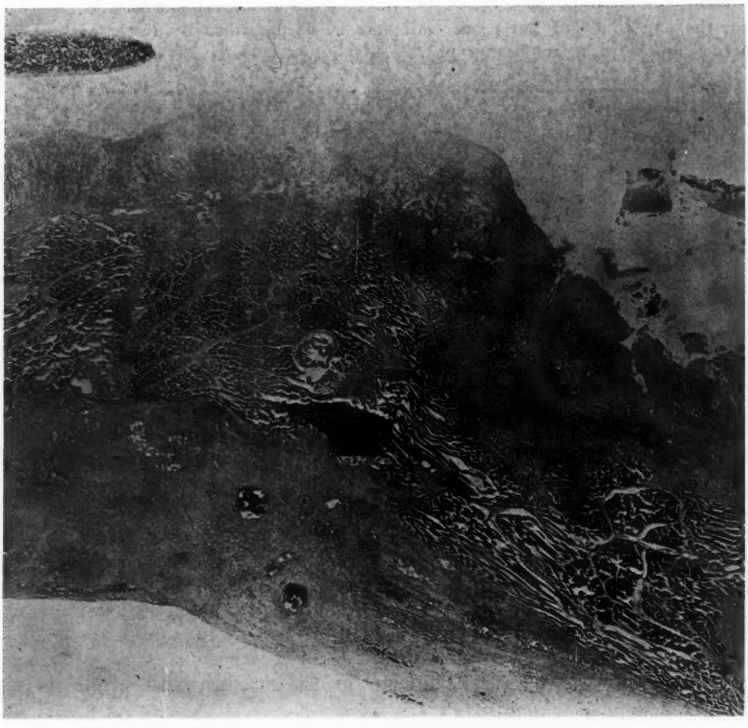

Fig. 2.—Section with low magnification, through the wall of the specimen seen in Fig. 1. Edema, necrosis, with no evidence of replacement.

Gins[20] had described this effect as due to the death of epithelium and the liberation of lytic enzymes. Silverberg and Voit,[37] in 1932, discussed the occurrence of thymonucleic acid in transplanted tissues, suggesting it as a factor. Cain,[38] in 1943, recognizing the problem of coagulation necrosis suffered by tissue transplants, felt it due to enzymes and reported the use of oxalate and enzyme poisons, to inhibit this sequence of events.

This coagulation and liquefaction of our transplants was anticipated. A preserved transplant was then decided upon, from which as much of the mucosa as possible and adherent peritracheal tissue had been removed. It was felt this transplant would offer

purely a superstructure for the ingrowth of respiratory epithelium, connective tissue, and possibly cartilage. Also, this type of graft was nonviable, would cause much less severe local tissue reaction in the host, and present a greater chance for successful use.

A dog was anesthetized and the trachea removed under aseptic conditions. The membranous portion of the trachea was completely removed and as much as possible of the mucosa from the cartilagenous portion. The thin layer of vascular and connective tissue intimately adherent to the outer surface was removed. This, in effect, left only the cartilage of the trachea supported by the perichondrium and intercartilagenous fibromuscular framework. Fig. 3 represents such a graft. The specimen was then placed in a solution containing equal parts of sterile saline and aqueous Merthiolate. To this was added 500,000 units of aqueous penicillin. After refrigeration for twenty-four hours sterile cultures were obtained from the solutions in two-thirds of the cases. The specimens were replaced in fresh solutions and allowed to remain refrigerated for another twenty-four hours. The solutions were then uniformly sterile. The solutions were brought slowly up to room temperature before culturing. If the trachea was to be kept longer before use, as a transplant, it was placed in a third fresh solution and placed in the deep freeze, where it became suspended in a block of ice.

Fig. 3.—Homogenous, preserved, tracheal transplant that has been partially de-epithelialized.

The transplants were preserved in the solutions for two reasons.

1. The washing and dilution effect on the bacteria present.
2. The washing and dilution effect on the enzymes present.

The transplants were used at time intervals up to three weeks. The interval difference up to this length of time seemed to have no bearing on the success or failure of the transplant.

Standardization of Surgical Procedure.—A number of dogs were used before arriving at a practical and workable method of securing the transplants in place in the host. At first, simple end-to-end anastomoses of the graft to the trachea were performed. These dogs began to present symptoms of tracheal obstruction around the tenth to fourteenh days. Tracheoscopy revealed the grafted portion to be edematous and tortuous, and the lumen to be angulated at both suture lines. The rigid ends of the trachea of the host seemed to exert a hinge effect on the softer graft. It was felt that during this early period, when the sutures no longer held the graft tightly, any movements of the neck or filling of the esophagus tended to displace the transplanted portion off the direct line of tracheal continuity. Such a situation was abetted by the softening of the graft. There-

fore a different type of anastomosis was instituted. To overcome to some extent the hinge effect a "sleeve" type anastomosis was performed as illustrated in Fig. 4. This type of anastomosis was used in all the dogs in Group 2.

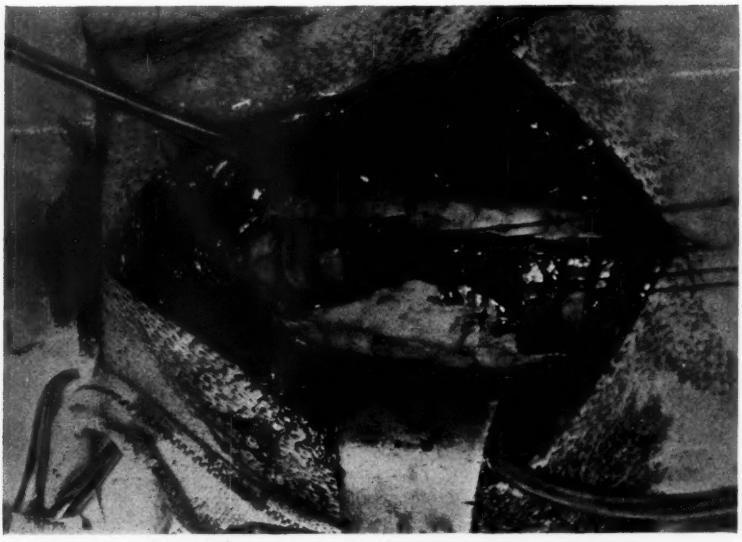

Fig. 4.—Graft in place with "sleeve" type anastomosis as used in Group 2.

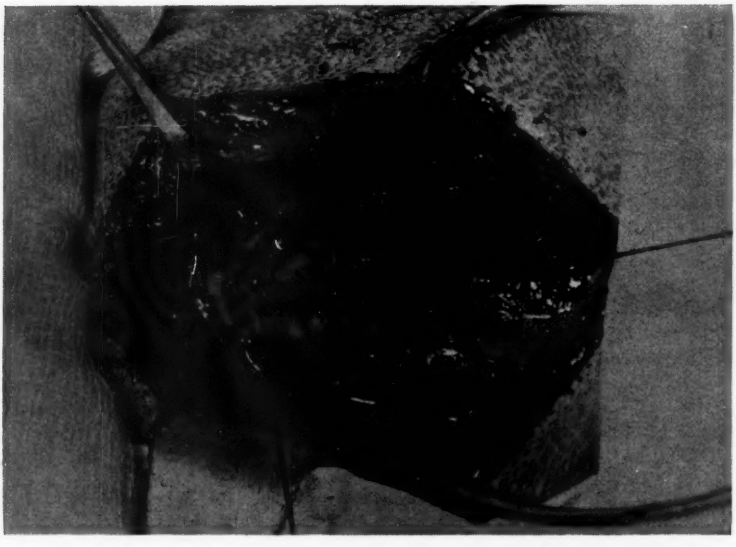

Fig. 5.—Completion of "sleeve" type anastomosis as used in Group 2.

To allow for any disproportion in the size of the trachea, transplants from large tracheas were used in medium- and small-sized animals. Several sizes were always available and not chosen until the host's neck had been opened and the trachea inspected. A selected portion of the trachea was then carefully dissected, care being taken to preserve as much of the peritracheal vascular tissue as possible. The segment to be removed (complete cylinders from one-half to one inch in length) were resected. The transplant was then slipped under both ends of the remaining trachea so that there was an overlap of from one-fourth to one-half inch. The open portion of the transplant was lying in the anterior midline. Both ends were then sutured over the host's trachea using two rows of interrupted 0000 silk at each extremity. The midline of the transplant was then closed with a longitudinal row of interrupted 0000 silk. The strap muscles of the neck were approximated over the area to act as a seal, and also as part of the outer framework of the newly formed trachea itself. Fig. 5 shows the appearance of this type of anastomosis at completion. This procedure circumvented to some extent the mechanical difficulty of sagging in of grafts up to one inch in length and became established as the method of choice in this type of transplantation in the trachea.

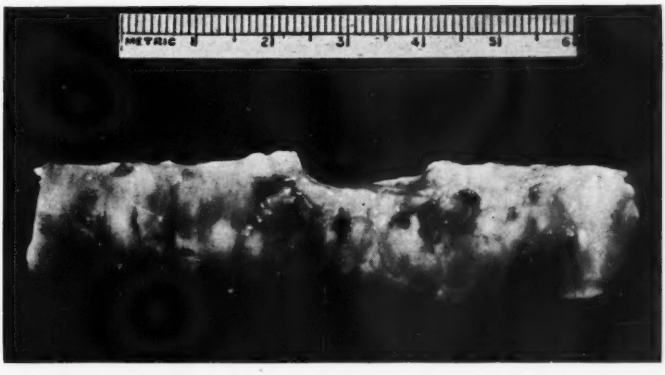

Fig. 6.—Window defect created five months before and closed with preserved transplant. Note loss of symmetry and absence of rings over the grafted area.

Group 1.—In this group five dogs were used.

Square windows were cut from the cartilagenous portion of the trachea measuring approximately one-half of the circumference, the size depending on the size of the trachea. A preserved transplant was put in place using simple end-to-end anastomosis. The postoperative course was uneventful. The dogs were not given penicillin. The only symptoms present were a mild cough and some loss of appetite. They started eating regularly in several days, and the cough disappeared in the second and third weeks. All dogs survived and were sacrificed at periods varying from three weeks to ten months. In two of the dogs transplants were used in the left main bronchus as well as the trachea.

At three weeks the transplant was soft and semirigid. It was thickened and edematous and densely adherent to the neck muscles and surrounding tissues. Microscopic study revealed respiratory epithelium growing in from the edges and covering at least one-half of the graft. Within six weeks it was completely covered. At three weeks there was marked edema of the submucosa.

There was an early ingrowth of fibroblasts which were arranged in linear fashion. The cartilage in the transplants stained pink and retained little of its normal bluish color. A layer of granulation tissue was present on the inner surface of the graft and there was a dense infiltration of lymphocytes of the small round type.

Present also were a smaller number of polymorphonuclear leucocytes. At three months there was considerable thinning of the wall of the graft. The neck muscles were directly adherent to this area preventing to a great extent collapsing of the segment into the tracheal lumen. This was held to be purely a mechanical advantage. The muscle formed a firm wall on which the transplant lay, held taut by the tracheal edges. At five months it was impossible to identify the site of anastomosis from the mucosal surface. This could be readily identified from the outer surface however, due to the loss of symmetry and the absence of cartilage rings. Fig. 6 presents such a specimen. One can readily identify the site and extent of the grafted area.

Sections revealed the wall to be very highly vascular during the first three months, but then gradually to thin out and form dense scar tissue. In two specimens there were small areas of calcification in the graft.

All of the animals in this experiment responded well to the grafts. There was no mortality nor was there enough stenosis of the airway to incapacitate the dogs. There was loss of tracheal symmetry at the graft site but this was not a serious effect. One could say that small window defects were successfully closed with preserved tracheal grafts, in animals in which up to one-half of the wall was removed (cartilagenous portion). This was true of bronchial as well as tracheal specimens.

Group 2.—Thirteen animals were used in this series.

All anastomoses were performed as described in Fig. 4. In five consecutive animals one-inch sections were removed and tracheal continuity restored with preserved transplants. All dogs survived and were sacrificed at intervals varying from three weeks to ten months. Gross and microscopic observations were similar to those in Group 1. At three weeks there was growth of respiratory epithelium from the tracheal edges toward the center of the graft. The most central epithelial growth was low columnar in type without cilia. The epithelium near the anastomotic site was mature and ciliated. At six weeks the graft was almost completely epithelialized, and at three months covering with mature ciliated respiratory epithelium was complete. Fig. 7 is a section through the wall showing this epithelium, scar tissue in the wall and absence of cartilage.

The presence of submucosal edema during the first six weeks was constant. Between the columns of ingrowing epithelium, there was granulation tissue. The tissue was markedly edematous, containing a large number of segmented leucocytes but also a high percentage of small lymphocytes. The cartilage was rapidly disappearing at six weeks and at three months, as seen in Fig. 7, was entirely replaced by scar. The wall at this interval was thick and good tracheal continuity was maintained though there was some tendency to sag inward.

At six months, as seen in Fig. 8, the wall of the trachea in the area of the transplant was much thinner than at three months. There was complete absence of cartilage and the scar tissue in the wall was less thick. The neck muscles were

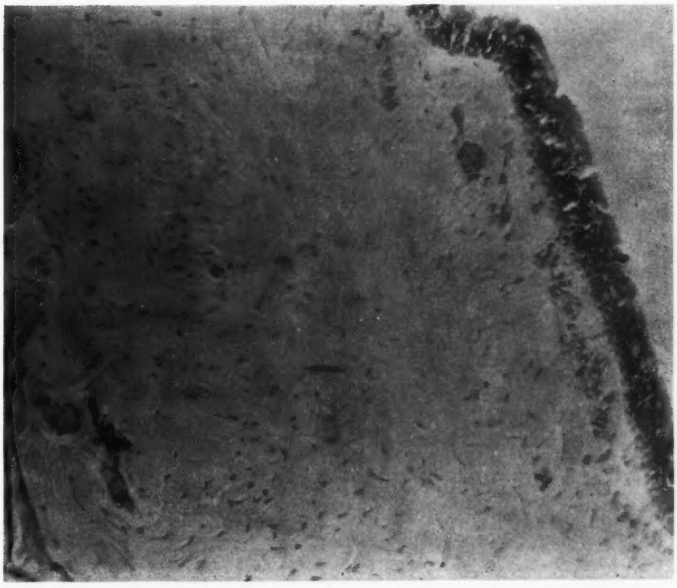

Fig. 7.—Section under high magnification. Graft three months old. Mature respiratory epithelium, dense scar in the wall with absence of muscle and cartilage.

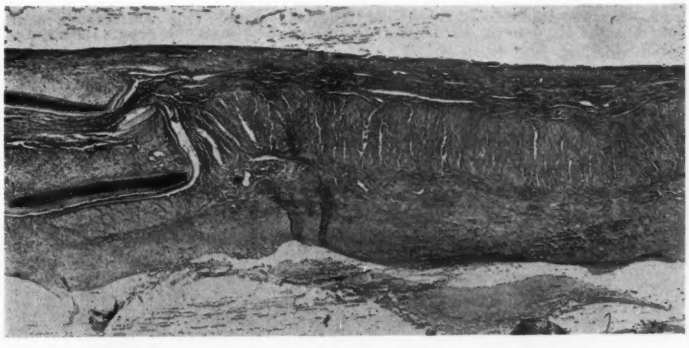

Fig. 8.—Appearance of transplant after six months, under low power magnification. Complete epithelialization. Note normal tracheal cartilage at left extremity. The wall is thinner than at three months.

dissected from the specimen before photographing but it is felt that this musculature played an important role up to this interval in maintaining the integrity and patency of the tracheal wall in the area of the transplants.

At six months there was a definite tendency to sagging inwards of the grafted area with a loss of from one-fourth to one-third of the lumen of the trachea. This was undoubtedly due to retraction of the scar tissue and gradual thinning of the tracheal wall.

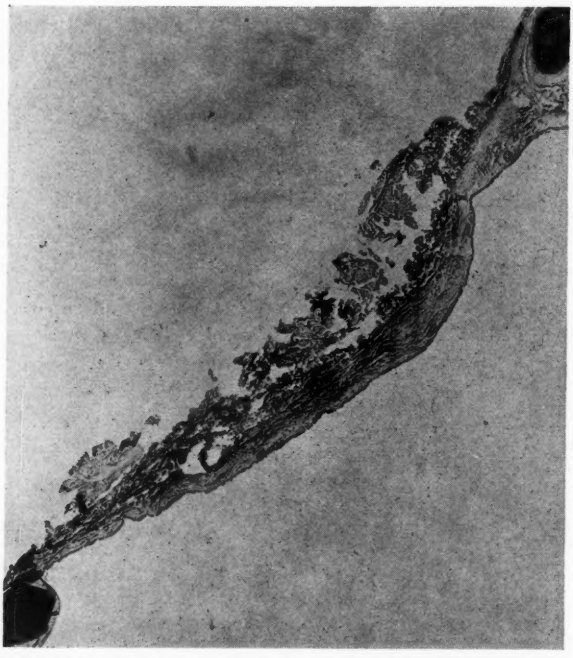

Fig. 9.—Marked thinning of the wall of the transplant. This is after ten months in the host. Neck muscles have been dissected from the wall. Cartilage seen is from the trachea of the host.

Fig. 10.—Gross specimen of the section seen in Fig. 9. The extent of the graft is readily identifiable. This is ten months after transplantation.

At ten months the wall was thinner and there was further loss of tracheal lumen, extending from one-third to one-half of the circumference. Fig. 9 presents a section of the wall at this interval. At either extremity one can see

normal tracheal rings which are not a part of the transplant. There is no cartilage present in the graft. Fig. 10 presents the gross appearance of this trachea. The extent of the transplant is easily identified. The dog was not incapacitated in his usual activities around the pen but his activities were restricted by the pen.

In three dogs one and one-half inch segments were removed and transplants put in place. Two of these died during the third week, of strangulation while eating. They were coughing and had been ill since the first week, loosing weight steadily. They were noted to have difficulty in breathing. Both strangled while eating during the third week. Autopsy revealed the trachea in the transplanted area to be extremely soft, pliable, and easily compressed. There was marked sagging inward of the wall reducing the lumen to less than one-half of its normal size. It was felt that the esophagus, filled with a bolus of food, had closed off the trachea completely. The remaining dog was sacrificed at ten months. The microscopic findings were similar to those previously described. However there was a significant loss of tracheal lumen, it being only one-half its normal size. The wall was thin, tough, and fibrous. No cartilage was present, it was easily compressed and it seemed that but for the effect of the neck muscles a fatal obstruction would have occurred early in the postoperative course.

Using four consecutive dogs, two-inch sections were removed and the transplants used to rebridge the defects. All of these dogs coughed severely during the first week, ate very little, and were ill. All four died during the second and third week; three of strangulation while eating and one during the night. Gross examinations revealed a severe sagging inward of the tracheal wall at the transplant site. This portion was a soft, flaccid tube. It was felt that the sagging was of a mechanical nature much the same as a clothesline which, though suspended at either end sags in the middle.

DISCUSSION

The achievement strived for in these experiments was to bridge extensive defects in the trachea, or tracheobronchial segment. It was hoped that long lengths could be resected and continuity be re-established using homogenous tracheal transplants. Our experiments have failed to produce these results. An experimentally successful transplanting should satisfy the following criteria to be deemed worth while.

1. The transplant should become an integral part of the system anatomically.
2. It must satisfactorily meet the functional requirements.
3. A minimum of morbidity should accompany its use.
4. It should present a permanent replacement.

It was wished by us, to accomplish this without the use of foreign materials that might require removal later.

Our failure to meet the preceding criteria is obvious from study of the experiments. Small window defects were successfully closed using these trans-

plants. However, such defects have been covered by others using fascia, plastics, and Gelfoam. The producing of a framework for the ingrowth of tissue was the important factor in these repairs. The repaired portion was not rigid and there was loss of tracheal symmetry. When the defect was not extensive or did not involve over one-half of the cartilaginous portion of the trachea, there was not sufficient loss of luminal circumference to encroach on function. The transplants were covered inside by the ingrowth of epithelium from the ends of the trachea. The cartilage and fibrous tissue within the walls of the grafts slowly underwent liquefaction, absorption, and replacement by scar tissue.

In the experimental animal temporary success was attained in the closure of short complete tracheal defects in lengths not greater than one inch. Histologically and anatomically the same succession of events, as described in the small window defects, were found. Edema, liquefaction, absorption, and subsequent replacement by scar was the succession. Respiratory epithelium readily grew in over the graft from both ends of the trachea and within three months the graft was completely covered. At six weeks there was marked degeneration of cartilage in the graft; at three months there was fibrosis where the cartilage had been. In none of the specimens was there any evidence of regeneration of cartilage within the wall, or of growth from the trachea into the transplant.

As the cartilage disappeared, the transplant became a nonrigid tube lined with respiratory epithelium whose patency was maintained by the suspension effect of the rigid ends of the trachea, and the neck musculature. These muscles were markedly adherent to the wall and actually formed an integral part of it. When they were dissected away from the transplant, the wall partially collapsed. At six months there was a loss of from one-fourth to one-third of the tracheal lumen; at ten months from one-third to one-half was lost. The scar tissue though thick in the first months, thinned out markedly at six and ten months.

When the defect was increased to one and one-half inches in three dogs, two died within three weeks of tracheal obstruction. When this was increased to two inches in four dogs, all died within three weeks. The most common finding was strangulation while eating, though two died during the night. Study of the specimens revealed a soft, edematous, flaccid tube, without support. That fatal obstruction did not occur in the cases where shorter segments were removed was thought to be due to the suspension effect of the divided ends of the animal's trachea and the stabilizing effect of the neck musculature. In other words where longer transplants were used, the resulting flaccid tube was too long for these factors to support and complete early obstruction was inevitable.

In summary it can be said that by the methods used in these experiments, short segments can be transplanted and a soft fibrous tube lined with epithelium up to one inch in length can be produced. However, there follows a gradual narrowing of this segment that will finally lead to obstruction.

It becomes necessary to provide a rigid framework for the formed tubes to prevent their gradual collapse. If this can be done, then the use of homogenous preserved transplants may possibly be successful. Further experimental work on this subject is at present being carried out by us using various materials.

Our experience indicates that a preserved homogenous graft is superior to a fresh one. This seems true due to the milder tissue reaction in the host and less tendency to massive liquefaction. There is a retarding of these processes with the use of preserved, nonviable, homogenous transplants.

CONCLUSIONS

1. Experiments have been reported in detail using homogenous tracheal transplants in the repair of tracheal defects.

2. The end results have been a failure in the repair of extensive defects due to the absorption and nonreplacement of cartilage, leaving a flaccid fibrous tube that eventually collapsed sufficiently to cause tracheal obstruction. Some temporary success was obtained in repair of short defects due to the suspension effect of the ends of the animal's trachea and the neck musculature.

3. There was no evidence of generation or regeneration of cartilage in or into the transplanted segment.

4. A method of preservation of transplants is described.

5. The use of preserved tracheal transplants is preferred to those in the fresh state.

6. A technique for securing the transplants in place which is felt to be preferable to simple end-to-end anastomosis is described in detail.

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(See discussion on page 647.)

RESECTION OF THE TRACHEA AND BRONCHI

An Experimental Study

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THORACIC surgeons have been plagued by the technical problems concerned with the surgical treatment of tumors and strictures involving the trachea and major bronchi. There have been two principal obstacles to resection; first, the maintenance of an adequate airway during the operative procedure and second, the reconstruction of the segment so that it may resume normal physiologic function.

Malignant tumors extending into the carina, adenomas extending from a purely lobar origin into a main-stem bronchus, and various types of bronchostenosis constitute commonly encountered situations where reconstructive procedures could conceivably restore function without undue sacrifice of pulmonary tissue. A review of these problems and a survey of the experimental efforts of others, have suggested criteria which must be satisfied if physiologically adequate tracheal or bronchial reconstructions are to be performed.

These criteria demand (1) that an adequate airway must be maintained to the lungs during the procedure with, at most, only a brief interruption of intrabronchial closed circuit anesthesia, (2) that an airtight reconstruction of the defect must be obtained, (3) that rigidity must be sufficient to avoid postoperative respiratory "flutter" at the site of repair, (4) that the reconstruction must facilitate a mucus-free postoperative period, (5) that healing must be complete without late stenosis, and (6) that there must be minimal bacterial contamination at operation.

HISTORICAL REVIEW

Taffel demonstrated in 1940 that small tracheal defects could be closed successfully with patches of fascia lata. The grafts, applied with interrupted silk sutures which did not penetrate the lumen of the trachea, did not remain viable but acted as a scaffold for invading fibroblasts.[1] Daniel, repeating these experiments, found that stenosis occurred in the grafted areas. Later, glass and stainless steel tubes were inserted into tracheal defects and regeneration of tissues occurred around these including new growth of cartilage as well as mucosa.[2] Grindlay, Clagett, and Moersch have used polyethylene tubing for experimental reconstruction of the trachea.[3] No cartilage was found in the regrown tracheal wall of five dogs examined one and one-half to eleven months postoperatively,

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but apparently little stenosis developed in most and retention of secretions was not a problem.[4] Clagett, Grindlay, and Moersch reported the use of polyethylene tubing in one human case without success.[5]

Hanlon reported the successful use of gelatin sponge for the closure of small experimentally produced defects in the bronchi of dogs.[6] Gough used alginate gels (seaweed preparations) for closing similar small defects during the surgical treatment of pulmonary tuberculosis in human beings.[7] End-to-end anastomosis of divided bronchi, both with and without excision of experimentally produced strictures, has been reported by Jackson and associates. They developed an everted cuff method of closure that appears satisfactory.[8]

However, in spite of advances toward a solution of the problem, no one of these methods fulfills all the criteria for a physiologically adequate tracheobronchial reconstruction. With these criteria in mind, we have conducted further animal experiments which have resulted in one solution of certain aspects of the problem.

METHOD AND MATERIAL

Eighteen mongrel dogs were used in this study and more than one operation was performed on some animals. Anesthesia was achieved with 6 per cent Nembutal solution intravenously and aseptic operating room technique was always observed. All operations were performed transpleurally using interrupted positive pressure oxygen insufflation through a simple endotracheal tube made airtight by gauze packing in the throat of the anesthetized animal.

Four types of experiments were performed. In the first series of four experiments, the airway was divided and reunited by interrupted silk sutures through all the layers around adjacent cartilage rings. Two of these animals survived a significant period, one for eight months and one for four and one-half months. Of those not surviving, one failed to recover from the anesthesia, and in the other the anastomosis of the trachea was insecure resulting in bilateral tension pneumothorax (Table I).

A Foley catheter was used as an airway in the first set of experiments. The balloon end was introduced as far as the carina so that the trachea could be manipulated at a point proximal to the balloon. This same method was used in the second set of three experiments wherein whole segments of the trachea were excised and the defects reconstructed with tantalum gauze lined by pleura or fascia. These experiments were technically difficult, air leaks were frequent, and the longest survival time of an animal was only seven days (Table II).

From the first series of experiments it became apparent that simple through-and-through sutures about adjacent cartilage rings were satisfactory and that an inlying tracheal tube placed prior to operation in the manner of a bronchospirometric catheter would permit manipulations with the trachea open. However, the problem of excision in the region of the carina, where many of the resectable pathologic lesions exist, together with a satisfactory method of plastic repair, remained to be solved.

An inlying tube, placed in the tracheal lumen through the operative wound, had been used in the last of the tantalum experiments with success. This tube was therefore used in the third set of ten experiments in which either pneumonectomy or lobectomy was performed. The resected bronchus was divided flush with its parent stem, sometimes removing a portion of the parent stem as well. The remaining aperture was then closed by applying a patch from the wall of a small bronchus in the resected lobe or lung. Patches were first applied to the outside of the defect and secured with interrupted sutures. Air leaks were frequent by this method. Later the grafts were tailored, placed inside the lumen of the affected bronchus, and secured with two interrupted sutures for closure with a continuous suture of fine silk. In this group of ten experiments there were four survivors, sacrificed at intervals from thirty-four days to nine months postoperatively (Table III).

TABLE I. DATA FROM FOUR EXPERIMENTS OF BRONCHIAL OR TRACHEAL DIVISION AND RESUTURE

EXPERIMENT NUMBER	PROCEDURE	SUTURES	SURVIVAL PERIOD	CAUSE OF DEATH	CONDITION OF OPERATIVE SITE	PENICILLIN	SURGICAL AIRWAY
D1 - E1	Right upper lobe bronchus, division and reanastomosis	Interrupted 00 silk	8 months 4 days	Reoperation on trachea	Well healed. No stenosis. Good mucosal lining	+	None
D2 - E2	Division one-half of trachea and resuture	Interrupted 00 silk	3 days	Technical failure of airway. Bilateral pneumothorax		+	Foley catheter
D3 - E3	Complete division of trachea and resuture	Interrupted 00 silk	4½ months	Sacrifice	No stenosis. Mucosa covered stutures	0	Foley catheter
D18 - E19	Removal three tracheal rings and resuture	Interrupted 000 silk	Did not recover from anesthesia			+	Rubber tube

TABLE II. DATA FROM THREE EXPERIMENTS OF TRACHEAL RESECTION AND TANTALUM GAUZE REPAIR

EXPERIMENT NUMBER	PROCEDURE	SUTURES	SURVIVAL PERIOD	CAUSE OF DEATH	PENICILLIN	SURGICAL AIRWAY
D4 - E4	Resection three tracheal rings—tantalum and pleural patch	Interrupted 00 silk	7 days	Pneumonia; obstruction due to narrowed tantalum repair	0	Foley catheter
D5 - E5	Resection two tracheal rings—tantalum and pleural patch	Interrupted 00 silk	1 day	Did not recover from anesthesia	0	Foley catheter
D6 - E6	Resection two tracheal rings—tantalum and fascia patch	Interrupted 00 silk	At operation	Leak and tension pneumothorax	0	Tube

TABLE III. DATA FROM TEN EXPERIMENTS OF LOBECTOMY OR PNEUMONECTOMY AND AUTOGRAFT REPAIR

EXPERIMENT NUMBER	PROCEDURE	SUTURES	SURVIVAL PERIOD	CAUSE OF DEATH	CONDITION OF OPERATIVE SITE	PENICILLIN	SURGICAL AIRWAY
D8 - E8	Right upper lobectomy. Autograft outside	Interrupted 000 silk	2 days	Leak; bilateral pneumothorax		0	Tube
D9 - E9	Left upper lobectomy. Autograft outside	Interrupted 000 silk	9 months	Sacrifice	No stenosis and sutures covered by mucosa	0	Tube
D10 - E10	Left pneumonectomy	Not completed	At operation	Cardiac arrest			Tube
D3 - E11	Left pneumonectomy. Autograft outside	Interrupted 000 silk	45 days	Sacrifice	Graft viable; no stenosis; sutures covered	0	Tube
D11 - E12	Right pneumonectomy. Autograft outside	Interrupted 000 silk	Did not recover from anesthesia. Tension pneumothorax				Tube
D12 - E13	Right upper lobectomy. Autograft inside	Continuous 00000 silk	34 days	Sacrifice	Graft viable; no stenosis; sutures covered	0	Tube
D13 - E14	Right pneumonectomy. Autograft inside	Continuous 00000 silk	At operation	Cardiac arrest			Tube
D14 - E15	Right pneumonectomy. Autograft inside	Continuous 000 silk	Day of operation	Incomplete expansion, left lung		+	Tube
D15 - E16	Left pneumonectomy. Autograft inside	Continuous 000 silk	Day of operation	Incomplete expansion, right lung		0	Tube
D16 - E17	Left pneumonectomy. Autograft inside	Continuous 0000 silk	51 days	Sacrifice	Graft viable; no stenosis (edges not well tailored, however)	0	Tube

TABLE IV. DATA FROM THREE EXPERIMENTS OF TRACHEAL RESECTION AND HOMOGRAFT REPAIR

EXPERIMENT NUMBER	PROCEDURE	SUTURES	SURVIVAL PERIOD	CAUSE OF DEATH	CONDITION OF OPERATIVE SITE	PENICILLIN	SURGICAL AIRWAY
D9 - E20	Resection of four tracheal rings. Insertion of three-ring fresh (two hour) homograft	Interrupted 000 silk plus Gelfoam	7 months 19 days	Sacrifice	Marked stenosis with fibrous replacement of homograft	+	Tube
D1 - E21	Resection of four tracheal rings. Insertion of four-ring homograft. (Iced 21 days at -4° C.)	Interrupted stay sutures. Continuous 000 silk	Died at conclusion of operation	Graft too small in diameter. Tube could not be removed		0	Tube
D20 - E22	Resection of three tracheal rings. Insertion of four-ring homograft. (Iced 51 days at -4° C.)	Interrupted stay sutures. Continuous 000 silk	Living four months postop. but with wheeze		Bronchoscopy at 45 days showed short granulations and suggestive early stenosis at graft site	+	Tube

In the final group of three experiments, resected portions of the trachea were replaced with complete tracheal homografts from donor animals. A fitted tube airway was introduced at operation as before. The grafts were held with four interrupted sutures while a continuous stitch was placed at each end to make an airtight seal. A fresh homograft, two hours old, was inserted in one of these experiments. Homografts, stored at -4° C. for twenty-one and fifty-one days, respectively, were used in the other two. One animal died because the donor tracheal segment was too small and the procedure was therefore technically impossible. Of the two surviving animals, one was sacrificed at seven and one-half months and the other is living and well five months postoperatively (Table IV).

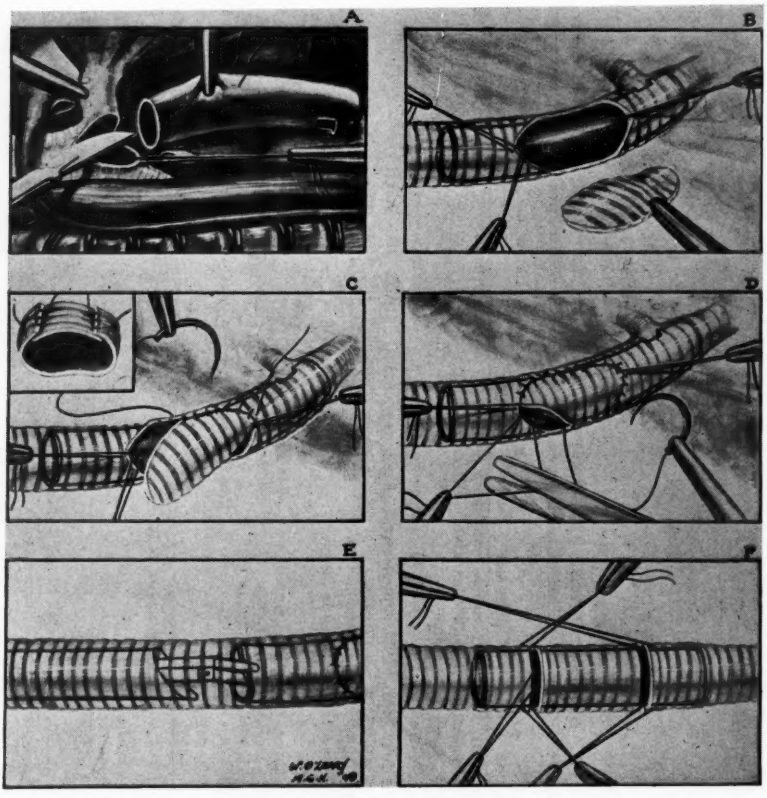

Fig. 1.—Drawing of the technique for insertion of a rubber airway tube and autograft in the radical resection of the right lung (dog). Drawings *A* through *E* illustrate right pneumonectomy as described in the text and *F* illustrates the use of the airway for resection of a complete segment of the trachea and its repair.

TECHNIQUE

For pneumonectomy, an anterolateral incision through the fourth intercostal space was used. A routine resection was performed with individual ligation and division of the hilar structures. The technique for insertion of the airway tube and repair with an autograft following right pneumonectomy is illustrated by the drawings in Fig. 1.

After the bronchus was cleared, an incision was made in the carinal angle sufficient to admit the rubber tube (Fig. 1, *A*). A guide suture of 000 Deknatel silk was placed on the

lower lip of the opposite main stem for its elevation during insertion of the rubber airway. A window was cut in the side of the airway near the distal end and a stay suture was looped through the wall of the tube on the side opposite the window. The tube was inserted from below upward until it lay within the tracheal lumen. Traction was then made both on the distal bronchial stay suture and on the tube traction suture so that the tube slipped down into the opposite main-stem bronchus where it lodged with the distal window opposite the left upper lobe orifice (Fig. 1, *B*).

When the division of the main stem was almost complete, a second traction suture was placed on the upper cut end and the resection completed. A graft was then fashioned from the cartilaginous portion of a bronchus in the resected lung. This was fitted with approximately two millimeters of overlap beyond the edges of the defect. A fine French needle was threaded on one end of the lower stay suture and this was used as the first anchoring stitch. A continuous suture of 000 or 0000 Deknatel was then started at the anchoring stitch. The sutures were placed from the inside of the defect outward and the edges of the graft were tucked under the edges of the defect so the graft lay within the tracheal lumen (Fig. 1, *C*). When the suture was complete on one side, an anchoring stitch was made from the second stay suture, and the continuous stitch was tied to this. The remaining circumference of the graft was then attached with a similar continuous suture. When only a small window remained, the traction suture on the tube was cut and removed (Fig. 1, *D*). The final stitches were placed and the reconstruction tested for leaks by covering it with saline while endotracheal positive pressure was made by the anesthetist. Rarely, a leak was found, and closed by a single stitch. A strip of Gelfoam was sometimes placed over the patch. The mediastinal pleura was closed over the site of the graft, the hemithorax irrigated, and the thoracic wound closed in routine fashion.

When the pressure in the hemithorax had been adjusted so that positive pressure anesthesia was no longer necessary, the Jackson bronchoscope was passed, the edge of the inlying rubber tube grasped with an ordinary biopsy forceps, and the tube and bronchoscope withdrawn together (Fig. 1, *E*).

Complete segment homografts were also placed in the trachea by the use of the inlying airway. The tube was inserted through the initial tracheal incision and stay sutures were placed on opposite sides of each cut end to counteract the normal tendency of the trachea to retract. After a segment of donor trachea was prepared, the distal (caudal) end of the tube was removed, the donor segment was slipped over it like a ring, the tube reinserted in the distal trachea and pulled into position by the traction suture. The stay sutures were first passed through the graft to secure it in position and a continuous stitch around adjacent cartilages completed the anastomosis at either end (Fig. 1, *F*).

Several technical points should be reviewed. A variety of tubes of graduated diameters was available for each operation. The tube selected was of a diameter to wedge snugly into the left main stem at the level of the left upper lobe orifice and it was of sufficient length to extend at least one and one-half inches beyond the upper margin of tracheal resection. The tube functioned as an internal tracheal splint by which the entire area could be elevated with traction on the tube suture. Furthermore, the tube then could not slip from the trachea or bronchus during repair, an accident which did occur early in the series. Since the tubes did not taper, slight leakage of air occurred on the tracheal end but this was readily compensated for by the anesthetist. The orifice in the tube opposite the left upper lobe bronchus was necessary to permit aeration of that lobe. The distal traction suture on the left main stem was imperative so that the edge could be elevated when the tube was drawn downward to glide into proper position. The method worked equally well for either lobectomy or pneumonectomy.

RESULTS

All experiments have been summarized in Tables I to IV. Complete healing occurred after division of either the trachea or bronchus and simple resuture

with interrupted silk. The sutures were covered by a cellular layer even in that portion which lay within the lumen of the trachea or bronchus and stenosis was never demonstrated (Fig. 2).

After resolution of technical difficulties, the method of autografts was found to work satisfactorily. Gross specimens from the surviving animals, taken after sacrifice, showed no stenosis of grafted areas following either lobectomy or pneumonectomy (Figs. 2 and 3). Microscopic examination of the grafts revealed firm healing with a minimum of inflammation, almost no fibrosis, and

Fig. 2.—Photograph of gross tracheal specimen from Dog 3; simple division and resuture of the trachea four and one-half months previously. Note firm healing without stenosis and cellular layer covering silk sutures (Experiment 3). A left pneumonectomy with autograft had been performed forty-five days prior to sacrifice. Note complete healing without stenosis (Experiment 11).

even viable cartilage in the transposed segments (Figs. 4 and 5). If the graft was poorly fitted outside the tracheal lumen, some granulations occurred with metaplasia of epithelium over these zones of malposition. In well-fitted grafts however, the epithelium retained its columnar and ciliated character even at the line of junction with the normal bronchus (Fig. 6). One badly fitted graft, with overlap on the interior of the trachea, nevertheless remained viable and

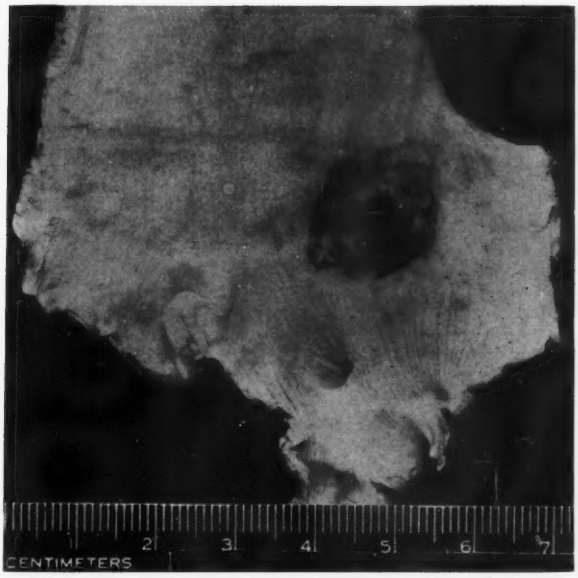

Fig. 3.—Photograph of gross specimen showing a poorly fitted autograft thirty-four days following a right upper lobectomy. The graft was viable but of unusual color since four hours elapsed from death to time of photograph (Experiment 13).

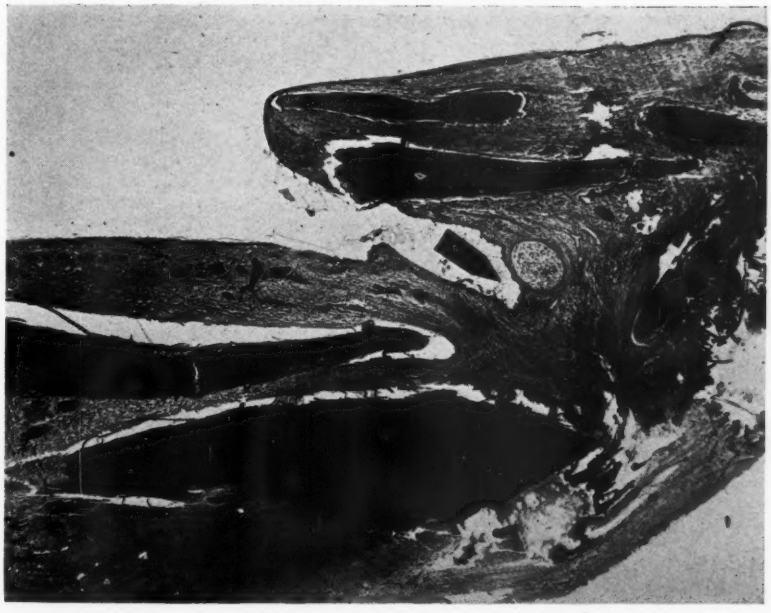

Fig. 4.—Photomicrograph of section of trachea and graft junction, right upper lobectomy, autograft inside, thirty-four days postoperatively (Experiment 13, gross, illustrated in Fig. 3). Note that in spite of overlap, the graft is viable, the union at arrow is firm and there is epithelium continuously over the upper (mucosal) surface. (Phloxine-methylene blue stain, ×40.)

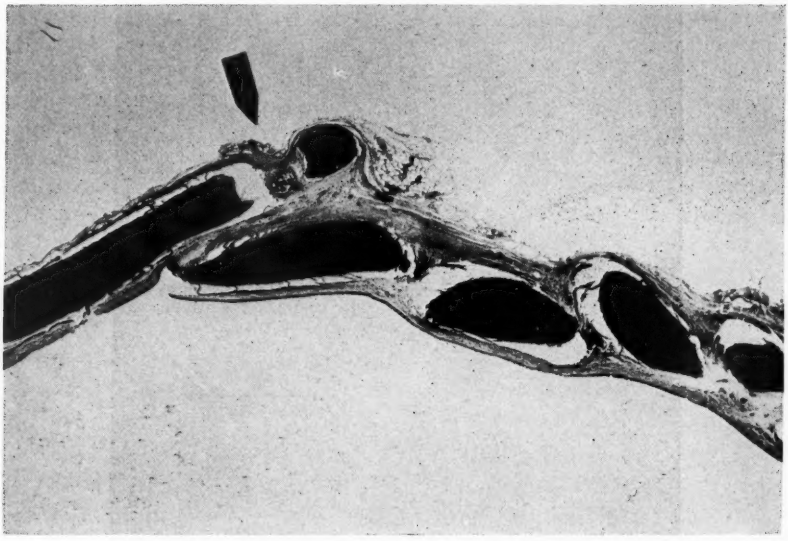

Fig. 5.—Photomicrograph of section of autograft placed inside lumen following left pneumonectomy fifty-one days previously (Experiment 17). Note integrity of entire graft, intact mucosa, except at junction where microtome caused artifact, and the simple resorption of a portion of tracheal cartilage where pierced by a silk suture, shown at arrow. (Phloxine-methylene blue stain, ×18.)

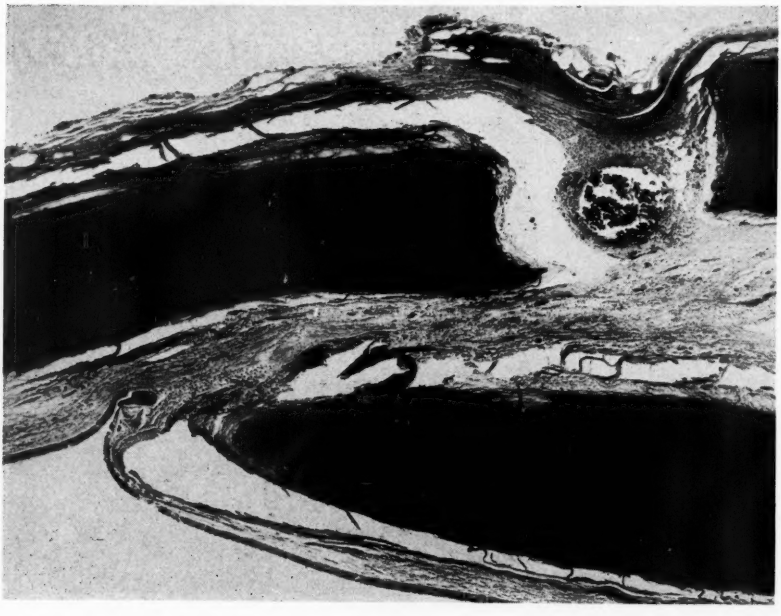

Fig. 6.—Photomicrograph at higher power of junction of autograft (below) with trachea (above), already shown in Fig. 6 (Experiment 17). Note firm healing, minimal inflammation, and the unusually normal ciliated columnar epithelium, even at the line of union. (Phloxine-methylene blue, ×50.)

Fig. 7.—Photomicrograph of center of autograft already shown in Figs. 3 and 4 (Experiment 13). Note viable normal epithelium and bronchial glands. A few mononucleated cells of chronic inflammation are present. (Phloxine-methylene blue, ×400.)

Fig. 8.—Photograph of gross specimen from Dog 9 showing marked stenosis of trachea at site of tracheal homograft seven and one-half months previously (Experiment 20). Intact left main-stem bronchus with autograft following left upper lobectomy nine months previously is seen at the lower right. Note lack of stenosis (Experiment 9).

its edges were covered by a proliferating pseudosquamous epithelium (Fig. 4), while in its central portions, the normal ciliated epithelium remained and even bronchial glands were retained (Fig. 7).

Of the two animals surviving homografts, only one was sacrificed. Prior to sacrifice the animal developed a marked wheeze and at autopsy there was pronounced tracheal stenosis caused by resorption of the homograft and replacement with fibrous and granulation tissue. The internal diameter of the lumen in the center of the graft was reduced to 0.5 cm. from a normal of 1.8 cm. in an interval of seven and one-half months (Fig. 8). Microscopically, death of the graft was evident with proliferation of granulation tissue, acute inflammation and metaplasia of the mucosa where it attempted to grow from the normal tissue to the graft (Fig. 9).

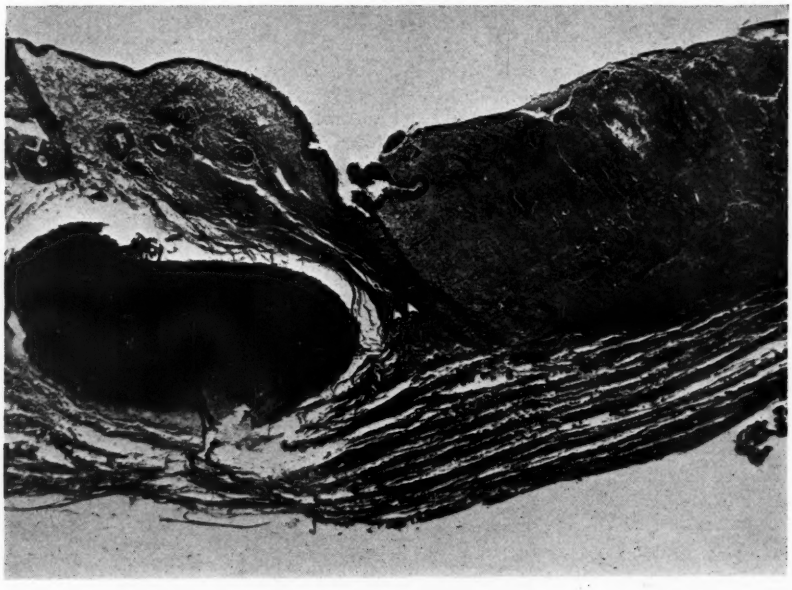

Fig. 9.—Photomicrograph of section of homograft shown in Fig. 8. Note replacement of graft by granulation tissue with fibrous proliferation on its external surface, seen at bottom of picture. Mucosal proliferation with marked metaplasia is present at the junction of normal trachea with replaced graft. (Phloxine-methylene blue, ×40.)

Bronchoscopy of the remaining homograft animal showed granulation tissue and slight stenosis occurring two months postoperatively although the dog was clinically well.*

In all experiments where an airway was placed in the trachea through the operative field, the tube was easily removed postoperatively with the bronchoscope.

*A respiratory wheeze was apparent in this animal four months after operation. This dog was used for a cardiac experiment performed by another investigator and the tracheal graft segment unfortunately was not saved. A portion of the trachea distal to the graft was preserved and this was normal.

The experiments with tantalum gauze failed because it was almost impossible to secure an airtight closure. However, they did confirm the impression gained in the first series of experiments, that a tube correctly placed would permit maneuvers to be performed on the opened trachea without undue haste.

Infection was not present in the pleural space of any animal although intrathoracic penicillin was used in only six of the twenty experiments. Antibiotics were not used by any other route. Bacteriologic cultures of small bits of tissue from the graft segments taken both before and after preservation by cold showed no growth.

Interruption of bronchial vessels and nerves incident to the complete dissection of bronchi or the trachea apparently did not adversely affect the healing process.

DISCUSSION

The radical resection of the lesions involving the carina or the opposite main-stem bronchus by insertion of glass and plastic tubes has heretofore been only partially successful. This maneuver must be done with great rapidity because of the serious consequences following anoxia of even very brief duration.[9] The method here described, using rubber tubes inserted through a small incision at the beginning of bronchial resection, offers a certain way of maintaining the flow of gases under positive pressure to the remaining pulmonary tissue while permitting careful dissection of the lesion. Further, the inlying airway acts as a prosthesis around which the bronchus or trachea may be more easily reconstructed. Postoperative removal of the tube eliminates the necessity for a permanent inlying foreign body.

Relatively large defects in a bronchus or trachea can be repaired by autografts in those cases in which pulmonary resection is performed. The objection raised at once is that the segment of resected lung might contain tumor or abscess so that either neoplastic disease or infection would prevent the use of smaller bronchi as grafts. This undoubtedly would be true occasionally. However, since the diameter of a tube is small compared to its circumference, grafts of a size adequate to repair a flush bronchial resection may be fashioned from bronchi of relatively high order, hence at a considerable distance from the primary lesion.

We suggest that a method is now available for bronchial reconstruction that is applicable to most situations requiring partial bronchial or carinal resection and which satisfies all of our originally established criteria. The insertion of a tube, removable at the conclusion of the operation, works equally well on either a lobar or main-stem bronchus and maintains a patent airway to the functioning pulmonary tissue with minimal leakage of air during the operation. An autograft, tailored and applied inside the lumen with a continuous suture, makes an airtight closure, has the firmness of normal trachea or bronchus without abnormal rigidity, offers the same mucosa-covered surface as normal bronchus for the retention of mucus during tussive effort, and heals firmly without fibrous stenosis. The preoperative preparation of an assortment of varying sized tubes which are introduced through the sterile operative wound rather than through

the mouth of the patient and the proper selection of an autograft from resected tissue provide a technique by which bacterial contamination may be kept at a minimum.

Possible clinical applications for this technique are at once apparent. A relatively benign tumor, such as bronchial adenoma, is occasionally found in such a situation that resection of the lung is necessary because of encroachment on the main-stem bronchus. This might be converted to a lobectomy with salvage of the main stem and remaining lobe or lobes. Occasionally a carcinoma is found growing from the main stem into the carina which is sufficiently localized that pneumonectomy would be feasible if a method of plastic repair were available for a hemisected opposite main stem. This method could not be interpreted as changing the ultimate cure rate of such lesions but, since these tumors usually obstruct completely and cause asphyxia or suppuration distal to the carina, worth-while palliation might be achieved. It should be possible in such cases to obtain a small area of bronchus free from tumor and without severe bacterial invasion in its walls, which could be adequately cleansed with saline to permit its use as a graft.

Benign strictures of a lobar or main-stem bronchus might be excised and end-to-end suture achieved by the use of an inlying tube. Indeed, Griffith ingeniously resected a simple stricture of the left main stem without such help,[10] and Tuttle anastomosed a left upper lobe bronchus directly to the left main stem following radical incision in a difficult lower lobectomy.[11] Gebauer reported the use of dermal grafts in the reconstruction of tuberculous bronchostenosis.[12] However, in a patient with borderline pulmonary function, the tube method might make repair possible when even temporary interruption of airflow to a lobe or lung would exclude surgery entirely. Finally, for those accidents of surgery when more extensive incision is made than intended, the method described might permit the surgeon to recoup his position without undue risk to the patient or loss of functioning pulmonary tissue.

Lesions of the trachea requiring complete excision of several rings are probably still best treated by previously described methods, notably that of Grindlay and his colleagues. Belsey reported an ingeniously handled case where all but a narrow strip of trachea was resected for an adenoma and repair effected with fascia lata over a framework of stainless steel wire.[13] No late follow-up is available. Recently, Rob and Bateman have successfully repaired a defect in the cervical trachea with tantalum gauze and fascia lata.[14] We hoped, rather skeptically, that homografts would remain viable. Although this is not so, they do offer an excellent method of immediate repair and function well for about four months. They are, of course, not clinically applicable at the present time. It is conceivable that a small tracheal lesion, involving no more than three or four cartilage rings, could be resected and end-to-end suture be performed over a tube. This has already been performed experimentally over plastic tubes which are allowed to remain in the trachea.[3]

The ease with which sections of trachea may be removed and the airway maintained with a tube placed at operation, demonstrates the usefulness of the method for testing other types of plastic repair. It is hoped that some adapta-

tion, possibly involving autografts with bronchus from a deliberately sacrificed lobe, will make resection of the isolated tracheal lesion an acceptable technical maneuver.

SUMMARY

A series of animal experiments have been performed to develop a method of radical bronchial resection and repair. Autografts with segments of bronchus from the resected lobe or lung, have been found to possess the correct characteristics for a satisfactory postoperative recovery in addition to remaining viable for complete healing without the development of fibrous stenosis.

The use of a rubber tube for the maintenance of an airway to the remaining lung at operation is described together with the technique of autograft repair.

Homografts of complete tracheal segments from donor animals, inserted by a similar technique, have been shown to function well through the immediate postoperative period but result in gradual resorption and the late development of fibrous stenosis at the site of repair.

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(See discussion on page 647.)

FURTHER EXPERIENCES WITH DERMAL GRAFTS FOR HEALED TUBERCULOUS STENOSIS OF THE BRONCHI AND TRACHEA

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WIRE-ENFORCED, dermal grafts have been used in eleven patients for the correction of severe, healed, tuberculous bronchostenosis or tracheal stenosis. The first four patients have been reported in detail.[1] Of the remaining seven patients, two had dermal grafts inserted in the trachea. In the first of these (Case 7), a separate, severe stenosis of the right bronchus was treated with a second dermal graft at the time of the tracheal operation. This patient has been reported.[2] The second patient had a right pneumonectomy, in addition to the tracheal graft, and died three days after operation. If pneumonectomy had been avoided, as in the first case, the result might have been favorable. Both of these patients have been reported in detail, with two other instances of severe, tracheal stenosis, to emphasize the differences in anesthesia and operative procedure, between bronchial and tracheal surgery.[3]

This paper is based on the whole experience. Its main object is to demonstrate the usefulness of wire-enforced dermal grafts, and to guide other surgeons in their application. Only those cases heretofore unreported are summarized, and the operative technique is not repeated.

Chart I supports the generally accepted fact that usually excisional surgery is required in severe, tuberculous bronchostenosis, but that successful collapse occasionally can be practiced. Also, it discloses a significant number of patients in whom a direct surgical attack on the bronchial lesion itself is indicated, thus permitting a salvage of lobes or lungs free of disease or healed.

Of 136 patients with definite tuberculous tracheobronchitis, 46 per cent came to surgical treatment. Undoubtedly some of the 20 per cent still under medical treatment will require future surgery. The chart possibly assigns a false importance to modern surgical treatment, for many of the surgical patients developed stenosis before the days of streptomycin. A limited experience to date indicates that future use of this substance and PAS will reduce the incidence of bronchostenosis, decrease its mortality, and the percentage of patients requiring surgery, and simultaneously increase the number healed by medical treatment alone. Conversely, the use of these items might enable patients to survive extensive disease, of a type ordinarily fatal without their use, and thereby increase the number requiring surgery and direct treatment of stenotic, tracheobronchial lesions. Nevertheless, it is felt that the administration of streptomycin and PAS, and other drugs likely to be forthcoming, will make tracheobronchial surgery unnecessary more times than it will cure patients to a point where surgery can be done. At this time, it is

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fitting to state that without streptomycin, PAS, or both, dermal grafts for tracheobronchial lesions probably would have a low incidence of success as far as tuberculosis is concerned. Therefore, it is believed that, whereas a definite field for dermal grafts and tracheobronchial surgery in the treatment of tuberculosis exists at the present time, it is likely to diminish because of present and future trends in medical treatment.

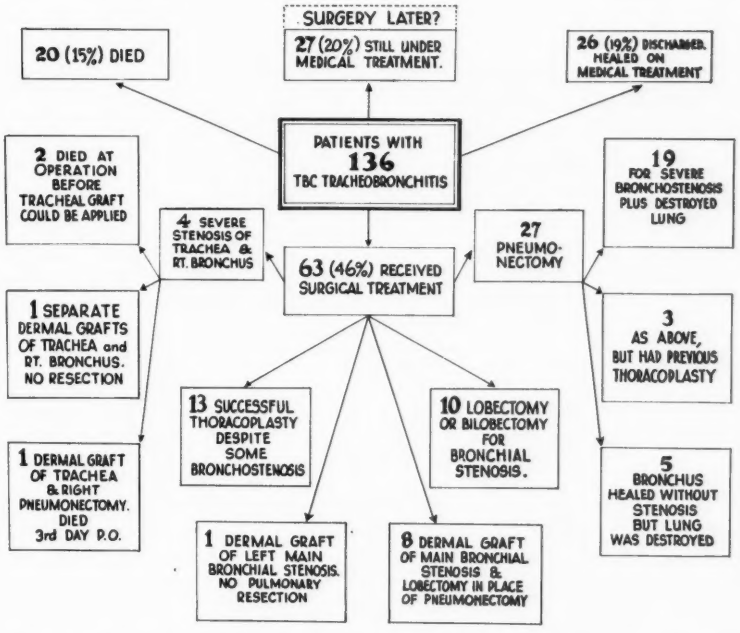
SURGERY LATER?
27 (20%) STILL UNDER MEDICAL TREATMENT.
20 (15%) DIED
26 (19%) DISCHARGED. HEALED ON MEDICAL TREATMENT
PATIENTS WITH 136 TBC TRACHEOBRONCHITIS
2 DIED AT OPERATION BEFORE TRACHEAL GRAFT COULD BE APPLIED
19 FOR SEVERE BRONCHOSTENOSIS PLUS DESTROYED LUNG
4 SEVERE STENOSIS OF TRACHEA & RT. BRONCHUS
27 PNEUMONECTOMY
63 (46%) RECEIVED SURGICAL TREATMENT
1 SEPARATE DERMAL GRAFTS OF TRACHEA and RT. BRONCHUS. NO RESECTION
3 AS ABOVE, BUT HAD PREVIOUS THORACOPLASTY
13 SUCCESSFUL THORACOPLASTY DESPITE SOME BRONCHOSTENOSIS
10 LOBECTOMY OR BILOBECTOMY FOR BRONCHIAL STENOSIS.
1 DERMAL GRAFT OF TRACHEA & RIGHT PNEUMONECTOMY. DIED 3rd DAY P.O.
5 BRONCHUS HEALED WITHOUT STENOSIS BUT LUNG WAS DESTROYED
1 DERMAL GRAFT OF LEFT MAIN BRONCHIAL STENOSIS. NO PULMONARY RESECTION
8 DERMAL GRAFT OF MAIN BRONCHIAL STENOSIS & LOBECTOMY IN PLACE OF PNEUMONECTOMY

Chart I.—Illustrates the fate of 136 patients with tuberculous tracheobronchitis, observed over a period of three and one-half years. The duration of disease varied from one to twenty years.

On the other hand, while personal experience, in man, with the use of dermal grafts for nontuberculous strictures, or for acute deformities resulting from the excision of malignant growths, is lacking, the applicability of dermal grafts in such instances should not be disregarded. A fibrous stricture of traumatic or nontuberculous origin may respond as well to a dermal graft as a healed, tuberculous stricture. In acute, traumatic, tracheobronchial defects, and those resulting from surgical excision, good results with dermal grafts might be expected, because they would be inserted in vascular, unscarred, normal tissues, and the adjacent respiratory epithelium would not be the loosely attached, atrophic and metaplastic membrane which lines healed, tuberculous stenoses. Usually acute, traumatic and excisional defects, in which partially intact cartilages persist, tend to gape and spread apart, rather than contract and close, as does an incised, fibroid stenosis. Nevertheless, the material used to fill such defects must have some semirigid support that will

maintain a normal caliber of the trachea or bronchus. During the healing period, the contraction of such defects is marked, and a large defect is certain to form a stenosis if an unsupported graft is used.

Perhaps, in time, dermal grafts will be used more frequently for nontuberculous, tracheobronchial lesions than for the tuberculous type. For the present, however, until a better method is discovered and becomes available, their use is earnestly recommended for the latter, and their trial strongly urged for the former. It is felt that greater use of dermal grafts will lead to such a discovery, or to significant improvements in all the methods so far used.

In general, experience to date indicates that wire-enforced, dermal grafts are a good means of correcting severe stenoses of the major bronchi and trachea. As time passes, the anatomic results seem to improve. The clinical results are particularly good from the beginning, with a loss or reduction of obstructive symptoms, better aeration by roentgenogram, and an increase in measured ventilatory capacity. Practically all the patients have professed marked, symptomatic relief, and improvement in their respiratory capacity. The first four patients[1] are well and at home. Two are active housekeepers, one is working, and one convalescing. In each of these patients, upper lobectomy and dermal graft of a stenosed bronchus to the remaining lobe or lobes was performed. Three were sputum-positive before operation and are now negative; the fourth is still negative, as before surgery. (The seventh and eleventh patients had tracheal grafts and will be mentioned later.)

The remaining five patients had bronchial grafts. They are summarized for the purpose of illustrating postoperative complications, criteria for the selection of patients, and technical aspects of the operative procedure, so that others may utilize this experience.

CASE REPORTS

CASE 5.—T. T., woman, aged 31 years. In July, 1947, when first seen, this patient had been hospitalized for six years. Following unsatisfactory right pneumothorax, pneumoperitoneum had been used for three years. Wheeze and sputum block first occurred in 1942, after a right phrenic paralysis, which became permanent when repeated one year later. Bronchoscopy in July, 1947, disclosed a severely scarred larynx, and extensive, ulcerocaseous tuberculosis of the lower trachea and right bronchial orifice. Streptomycin therapy was started and three months later the patient was transferred to Leahi Hospital for right pneumonectomy. However, the sputum became negative, and completion of the healing process in the lower trachea and right bronchus was observed bronchoscopically, until a clean, healed stenosis of the right bronchus at the carina was the only residuum. Breath sounds were diminished to absent in the right chest. Slight cough and wheeze were the only complaints. The roentgenograms (similar to Fig. 1, *A*) had shown no change for a long time. Because of few symptoms, negative sputum, and unchanging roentgenograms, right pneumonectomy was considered unjustified, especially in view of the uninvolved middle and lower lobes. She was discharged on Sept. 25, 1948.

Two months later, repeat bronchoscopy revealed a right bronchial lumen approximately 1 mm. in diameter. Wheeze and cough had become more troublesome. The sputum was still negative and the right middle and lower lobes were roentgenologically clear. The patient was readmitted. X-ray studies disclosed a heavy, diaphragmatic stenosis of the right bronchus at the carina (Fig. 1, *D*), some dilatation of the distal right bronchus, and an atelectatic right upper lobe which appeared as a dense cap over the apex (Fig. 1, *A*).

Right upper lobectomy and repair of the right main bronchus seemed to be clearly indicated. At operation, on Jan. 26, 1949, excision of the stenosis and suture of the intermediate bronchus to the trachea, did not appear feasible; the gap resulting from excision would have been too wide. Right upper lobectomy was carried out, and a short, wide, diamond-shaped, dermal graft was applied to the incised stenosis. This was difficult be-

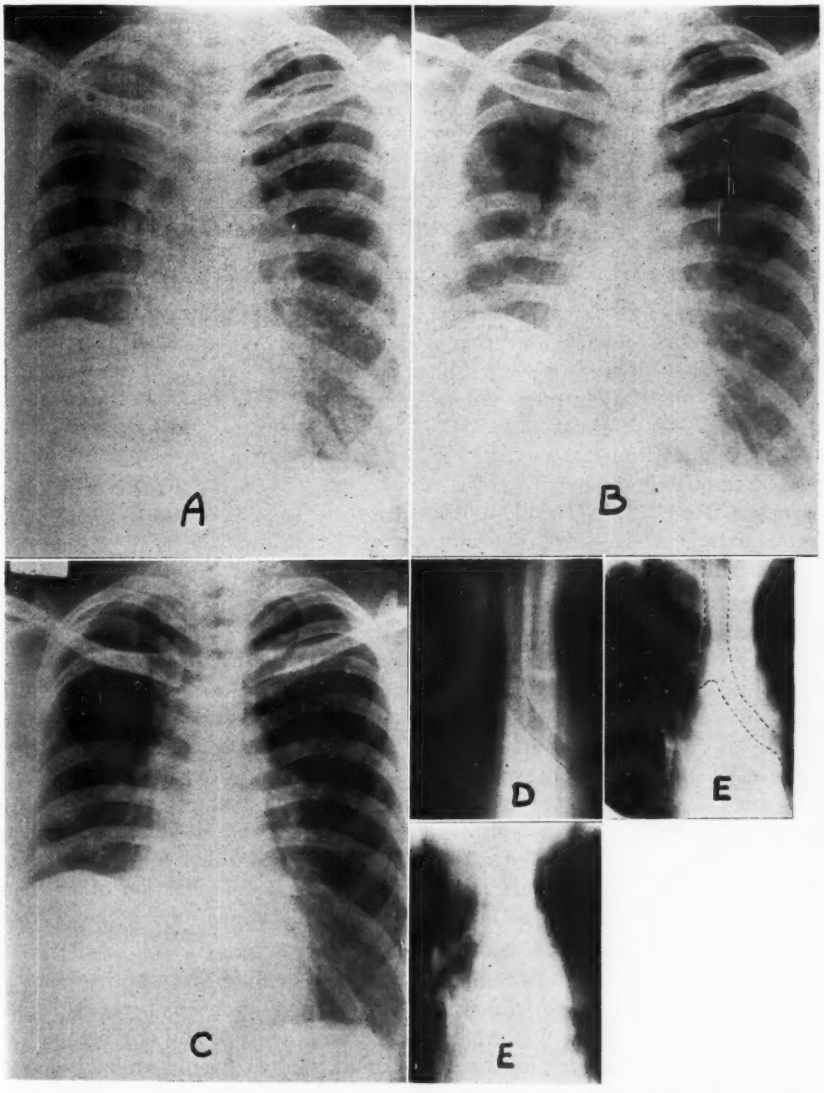

Fig. 1 (Case 5).—*A*, Before operation; permanent paralysis of right diaphragm, atelectasis right upper lobe. *B*, Five months after right upper lobectomy and dermal graft of right main bronchus. *C*, Eight months after operation, at time of discharge. *D*, Marked preoperative planigram. *E*, Marked and unmarked planigrams at the time of discharge.

cause of the nature of the stenosis. The short, heavy stenosis was hard to hold open. After being moulded to a round contour, the graft produced a large, posterior protrusion of the bronchial lumen, and the right bronchus was almost large enough to admit a finger. Postoperative recovery was entirely uneventful, except for hoarseness, secondary to laryngeal edema. Bronchoscopy, six weeks postoperatively, revealed a soft, edematous ring, 4 mm. in diameter, at the previous site of the stenosis. It was possible to worm the scope through it. The lumen beyond the carina was large, but the graft could not be identified. Everywhere the bronchial wall was smooth, clean, and pink. It is assumed that the stenosed portion of the bronchus pulled free from the graft, and attempted to reapproximate beneath it, with resulting recurrent stenosis. Planigrams (Fig. 1, *E*) showed the wire within the graft considerably posterior to the bronchial lumen. In the ensuing four months, six bronchoscopic dilatations were easily performed and a good lumen regained. Atelectasis did not occur (Fig. 1, *B*). Eight months after operation (Fig. 1, *C*), a clean, smooth, healed lumen, which admitted a bronchoscope with an external diameter of 7 mm., persisted, and the patient was discharged. No positive sputum cultures were obtained. One year after operation, the patient wrote, "I feel better and breathing is lots easier than before. Climbing steps was pretty much of a strain for me before the operation, but now I find it so much easier, and don't get out of breath as I did before."

Comment.—This fortunate result infers that it is not always necessary for a dermal graft to become a portion of the bronchial wall. Conceivably, it can function as a temporary seal of the enlarged airway, supply a framework, or scaffold for natural healing, and thus ultimately become an extrabronchial structure. However, such a method of bronchial repair is untrustworthy, and unappealing, the fortunate result in this instance notwithstanding. This case does exemplify the early tenacity of a dermal patch, for separation of the bronchus from the graft evidently did not occur until healing had progressed to an airtight state. It also demonstrates the healing and sealing qualities of the mediastinal structures.

It seems logical to conclude that, if possible, a short, weblike, or diaphragmatic stenosis should be treated by sleeve resection, as reported by Griffith.[4] The anxiety for a large airway encourages the use of wide grafts. The severity of the stenosis is proportional to the thickness of the bronchial wall. The thicker it is, the more it tends to curl back, and the harder it is to hold open. Too wide a graft produces undue transverse stretch on the bronchus; consequently the sutures cut through, as they do in all wounds closed with high tension, and the freed bronchial incision tends to reapproximate under the graft. It is probably better to err on the small side, rather than take this risk. Also, a small graft is more likely to take than a large one. On the other hand, when a graft fails to hold without complication other than the recurrence of stenosis, as in this instance, dilatations during the healing period may finally provide an adequate airway.

This patient is a good example of complete healing of an entire lobe by fibrosis and contraction, secondary to occlusion of its bronchus by healed scar. The clinical course of the upper lobe disease, and the gross and microscopic examinations of the removed lobe, indicated that it, alone, would probably never have caused trouble. The patient was reasonably well until the bronchial deformity reached a crucial point, productive of distressing symptoms, which arose from purely mechanical obstruction and were relieved by a mechanical procedure.

CASE 6.—F. Y., woman, aged 28 years. Admission x-ray film (Fig. 2, *A*), in 1944, showed an elevated right hilus from which a dense wedge extended to the apex, and scattered infiltration in the sub-apex. Extensive, ulcerocaseous tuberculosis of the lower trachea and right bronchial orifice was discovered at bronchoscopy. Despite this, a right phrenic crush was done for a spread to the right base. Incredibly, the base cleared and the sputum became negative. After eighteen months, the lower trachea and right bronchus showed considerable healing. The patient was discharged in 1946, after two years of hospitalization. Six months later, a sputum culture was positive. No x-ray change was noted, and no other positive findings occurred during a second admission of one year. This case was regarded, erroneously, as a possible instance of healing of the upper lobe by fibrosis, secondary to bronchial occlusion, as was demonstrated in Case 5.

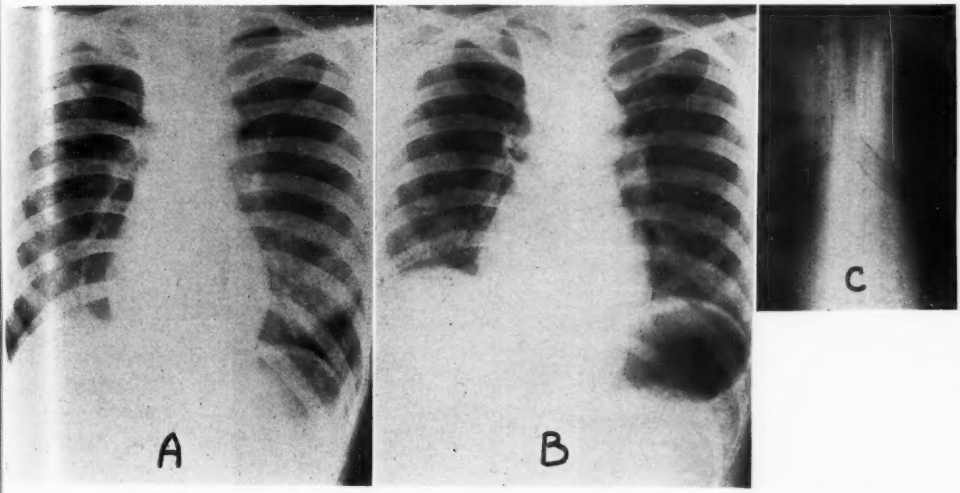

Fig. 2 (Case 6).—*A*, Admission roentgenograms, 1944: atelectasis right upper lobe, infiltration upper half of right lung field. *B*, Over four years later, just before operation: infiltration has cleared. *C*, Marked planigram before operation.

Six months after the second admission, increased wheeze and cough occurred, and the sputum became positive on smear. At bronchoscopy, the trachea appeared normal and there was a severe, healed stenosis of the right bronchus at the carina. There was no change radiologically (Fig. 2, *B*). Planigrams (Fig. 2, *C*) demonstrated probable occlusion of the upper lobe bronchus. Right pneumonectomy, or upper lobectomy and dermal graft of the main bronchus, seemed clearly indicated.

On Feb. 9, 1949, a dense, contracted, infiltrated and atelectatic, upper lobe was removed. No lumen could be demonstrated in its bronchus; active inflammation was later demonstrated by microscopic section. Opposite the upper lobe stump and at the carina, the opened right main bronchus had a lumen of 2 by 4 mm. There was no exudate; the lining was smooth, moist, and glistening. The middle and lower bronchi appeared normal, and both lobes were negative to palpation and inspection. A large, dermal graft was applied to the right bronchus.

The postoperative course was characterized by cough and a moderate bronchorrhea. Five months after operation (Fig. 3, *D*), the grafted bronchus seemed to be completely epithelized, and admitted a standard 7 by 40 bronchoscope. Shortly thereafter, the sputum became positive and there was evidence of fresh infiltration in the expanded right middle or lower lobes (Fig. 3, *E*). Sputum cultures were still sensitive to streptomycin; it was again administered, and PAS was added. By roentgenogram (Fig. 3, *F*), the infiltration in the lung cleared in one month, but cough and bronchorrhea increased; harsh breath sounds and

rhonchi became audible over the trachea and mid-upper chest. Bronchograms and bronchoscopy revealed a recurrent, tuberculous inflammation of the trachea, characterized by minute ulcerations and heaped-up projections of caseous exudate, and a fairy large, caseous mass in the lower trachea, obstructing the orifice of the left main bronchus. Much of this was removed with biopsy forceps. On section, the removed fragments proved to be granulation tissue. No tubercles were encountered. The grafted right bronchus showed no gross involvement. After bronchoscopy, there was marked symptomatic improvement. The

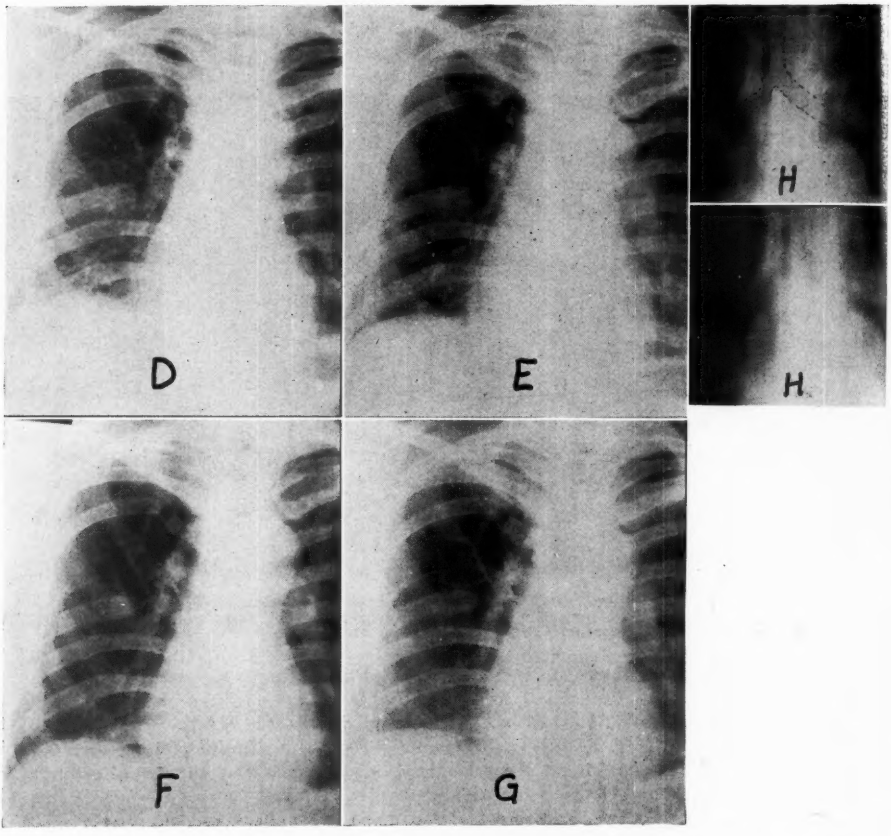

Fig. 3 (Case 6).—*D*, Five months after right upper lobectomy and dermal graft of the right main bronchus. *E*, One month later; fresh infiltration right upper lung field, recurrent, tuberculous tracheobronchitis. *F*, One month after *E*, six months after operation; clearing of infiltration (patient received PAS and a second course of streptomycin). *G*, Fourteen months after operation; sputum negative; good healing noted bronchoscospically. *H*, Planigrams marked and unmarked, at the same time. Bronchial lumen adequate. Wire within the graft was removed, bronchoscopically, eleven months after operation.

sputum converted to negative in three months, and has continued negative. Eleven months after operation, bronchoscopy showed practically complete healing but wire loops protruded into the tracheal lumen, just above the bifurcation, at the site of the previously-noted, caseous mass. Evidently, the recurrent tuberculosis had involved the tracheal portion of the graft. The wire loops were flattened with the tip of the scope; future cutting and removal were contemplated. A second, three-month course of PAS was started. One

month later, in January, 1950, the protruding loops of wire were cut and removed through a bronchoscope, whereupon additional wire loops became visible through a thin, filmy covering in the posterior wall of the proximal right bronchus. With more courage than skill, the wire was grasped with forceps, and completely extracted by a steady pull. There was little bleeding, and the right bronchial lumen remained open and unchanged.

The second course of PAS has just been completed. Fourteen months after operation, the bronchus appears healed, an adequate lumen is present and the chest film (Fig. 3, *G*) is clear. The patient is well; there is some cough, and about two ounces of mucoid sputum per day, which is negative. Planigrams (Fig. 3, *H*) show an adequate bronchial lumen.

Comment.—The ultimate result in this patient probably will be most acceptable. More cough and sputum than in other cases was present from the beginning. Although atelectasis never occurred, five months after operation a light spread of the disease, and a rather severe, recurrent tracheobronchitis did. All in all, the postoperative course was the least satisfactory of this experience. The availability of PAS was most fortunate, and it must be given credit for the result to date.

The removed lobe showed atelectasis, bronchiectasis, tuberculous infection in various stages of activity, and severe fibrosis—an entirely different picture from Case 5. There are probably many patients harboring healed, fibrosed, atelectatic lobes or segments similar to that removed in Case 5, which represents the ultimate in natural healing. On the other hand, it is pertinent to realize that, in the absence of positive sputum, there is no clinical or radiological means of differentiating such a lobe or segment from the type removed in Case 6. A small, dense, atelectatic lobe or segment, visible in an x-ray film, particularly if influenced by past or present collapse, is far from acceptable evidence of healing. They are a frequent source of future trouble, and are best removed, if there is the slightest laboratory or clinical evidence of activity.

This case points out that, despite long duration and every clinical evidence of healing, smouldering inflammation may persist in a healed, tuberculous bronchostenosis, and that following a graft, it may flare up when the effect of protective medication wears off. Fortunately, it is not a common event, and is highly improbable in the late, postoperative months. It can be partially avoided by carefully selecting patients and remembering that tuberculous bronchostenosis usually requires pulmonary resection. The preceding case is evidence that recurrent infection cannot always be avoided, inasmuch as the indications for dermal grafts in this patient were unquestioned.

Certain general opinions regarding the selection of patients have been formulated from the experience to date. Naturally, their revision may be necessary in the future, as more grafts are done. Healed, tuberculous tracheobronchitis is a relative state. Histologic evidence of activity is not a criterion of clinical healing; it may be found in lesions known to be years old, yet difficult to find in other lesions which were ulcerocaseous only a year before. Such lesions rarely heal in less than one year, and they are the type that result in stenosis. It is better, therefore, to wait at least a year after gross evidence of acute, destructive inflammation, before considering a graft. The procedure should not be attempted hurriedly, solely for the purpose of avoiding extension of the pulmonary disease, or the development of bronchiectasis.

Bronchoscopically, a healed stenosis appears clean, smooth, moist, and glistening. It appears lined with epithelium and the color is practically the same as near-by normal structures. Hyperemia indicates residual activity, or stasis, with distal secondary inflammation. The latter usually signifies the presence of bronchiectasis which is best treated by excision. Unlike true, caseous exudate, dried secretions accumulated on a clean base may not contraindicate surgery. Ordinarily, a single, stenotic lesion is usually in a uniform state, but unsuspected, gross evidences of activity in the bronchial wall may be encountered at operation, which call for resection. Therefore, it is better first to open and inspect the bronchus distal to the stenosis, before extending the incision through it into the trachea. Thus, if a graft is contraindicated and resection carried out, a repair of the airway above the stenosis will be avoided.

In three of eight instances of dermal grafts to healed stenosis of main bronchi plus lobectomy, the bronchus of the lobe removed was the site of caseous destruction at the level it was first circumsected. In each instance, satisfactorily healed, fibrous tissue was present more centrally, adjacent to the healed main bronchus, and bronchial closure was easily accomplished. None of these patients had recurrent or subsequent infection, although it is highly probable that some active foci existed within these main bronchi. Only grossly discernible lesions, such as areas of soft granulation, or caseation, when found in the bronchus to be grafted, contraindicate the procedure. Their presence in the bronchi of removed lobes is common, and their discovery in a lobar bronchus, at operation, does not signify that a graft of a stenosed main bronchus should not be done, unless the process extends centrally into the main bronchus. Valuable practice and experience in the appraisal of gross changes in diseased bronchi can be gathered by careful observation of the divided bronchus at every pulmonary resection, and the study of fresh, surgical specimens.

The gross pathologic changes of the bronchus observed at operations are most helpful in choosing between resection and bronchial graft, in contrast to the findings which concern the lobe or lung. They will be discussed after the next case which is rather illustrative.

The remaining feature, illustrated by the preceding case, signifies that, if recurrent infection occurs, the wire within the graft is likely to be a nuisance. Once healing is complete, a skeletal framework in the graft, for the purpose of maintaining bronchial patency, is probably unnecessary. However, in the absence of infection, the wire is not likely to be harmful so long as it remains imbedded in the graft. Also, at the time of grafting, and during healing, the dermal skin needs support to hold open the repaired bronchus, and to provide an airway for the residual lung or lobes. It is felt that any absorbable material, used in place of the wire, would greatly diminish the chances of success with dermal grafts, because cellular infiltration is essential for absorption.

Twenty-eight gauge wire, originally used, is heavier than necessary, and 30 gauge has been found more satisfactory. A finer gauge than this mght be

even better, especially if the incised bronchus can be held open easily. The smaller the wire, the easier it is to insert at a uniformly deep level in the graft. Kinks and irregularities are avoided more easily. If, after operation, cutting or removal of the wire should become necessary, it would be less difficult. Recurrent infection, as in Case No. 5, and placement of wire too near the epidermal surface, or the use of too heavy a wire which has irregular turns or kinks, and is difficult to mould properly, are the main causes for the postoperative appearance of the wire in the bronchial lumen. The periscapular skin of man is thick, and even after removal of the epidermis, the remaining dermal skin is frequently 3 mm. thick, or more, if it is not under tension. The inserted wire should be kept at least 1 mm. from the epidermal side. If the wire within the graft is visible through this surface, it is not deep enough. With wire no heavier than 30 gauge, the procedure is not difficult after a little practice. This is best done on fresh skin obtained from thoracoplasty patients. It is helpful to have the wire welded, in an "atraumatic" fashion, to a fine, cutting needle with a gentle curve.

CASE 8.—T. T., man, aged 30 years. In 1943, an army induction chest film showed a light, tuberculous infiltration in both apices, and more dense, scattered infiltration at the right base. Right pneumothorax produced atelectasis of the right lower lobe within nine months. It was discontinued and a right phrenic paralysis substituted. The sputum continued positive. Pneumoperitoneum was tried and abandoned because of severe wheeze. By January, 1945, the right lung had practically cleared and the right diaphragm resumed function. Shortly afterward, atelectasis and a massive spread occurred in the left lung, which increased initially, but, thereafter, never changed significantly. Bronchoscopy was first done in July, 1945, and showed "hyperplastic involvement" of both main bronchi. Early in 1948, a 120 Gm. course of streptomycin produced marked symptomatic improvement and converted the sputum for six months. There was no radiologic change. Bronchoscopy, in October, 1948, revealed hyperemia and occasional flecks of exudate in the right bronchus, and a healed stenosis of the distal left bronchus. The patient was transferred to Leahi Hospital for further study and possible left pneumonectomy.

There was exertional dyspnea. The left lung appeared to be destroyed (Fig. 4, *A*). Planigrams showed stenosis of the distal left bronchus (Fig. 4, *D*). The upper lobe bronchus could not be demonstrated. Sputum cultures were still sensitive to streptomycin. The patient's respiratory reserve was limited. Ventilatory studies showed a 1:1.7 ratio of tidal to vital capacities. They were 800 c.c. and 1,400 c.c., respectively. Bronchoscopy, in March, 1949, showed no change on the left, and the right appeared normal. Left pneumonectomy was advised only because an insignificant reduction in respiratory function was expected from removal of the diseased left lung.

At operation, on April 29, 1949, all the disease seemed to be confined to the upper lobe. The lower lobe was normal to inspection and palpation, and the fissure was practically free. The lower lobe did not collapse; it was compressed manually, and the upper lobe was removed. A short, fibrous, bronchial stump, in which a lumen could not be found, was sutured. Just distal to the point of division, the upper lobe bronchi were markedly dilated. The distal portion of the left main bronchus was then incised through the stenosis. It appeared healed and was lined with thin mucosa. Opposite the upper lobe stump, the lumen measured 3 mm. The left main bronchus, above the stenosis, contained a shallow, pouchlike, anterior protrusion, where the cartilages were intact. All the deformity of the stenosis was formed by the intrusion of the lateral and anterior bronchial walls. The appearance of the lower lobe branch bronchi did not suggest bronchiectasis; however, palpation now disclosed induration deep in the lobe, along the bronchovascular structures.

Ordinarily, such findings would indicate resection. In this case, it was felt that equally extensive induration probably existed in the right lung, because of previous disease visible in the early x-ray films. Also, a gamble for the function of a lobe seemed justified because of the patient's questionable preoperative respiratory function. Therefore, the left lower lobe was not removed, and the distal left bronchus was repaired with a dermal graft. A limited, modified thoracoplasty, designed to prevent overdistension of the remaining lobe, was carried out.

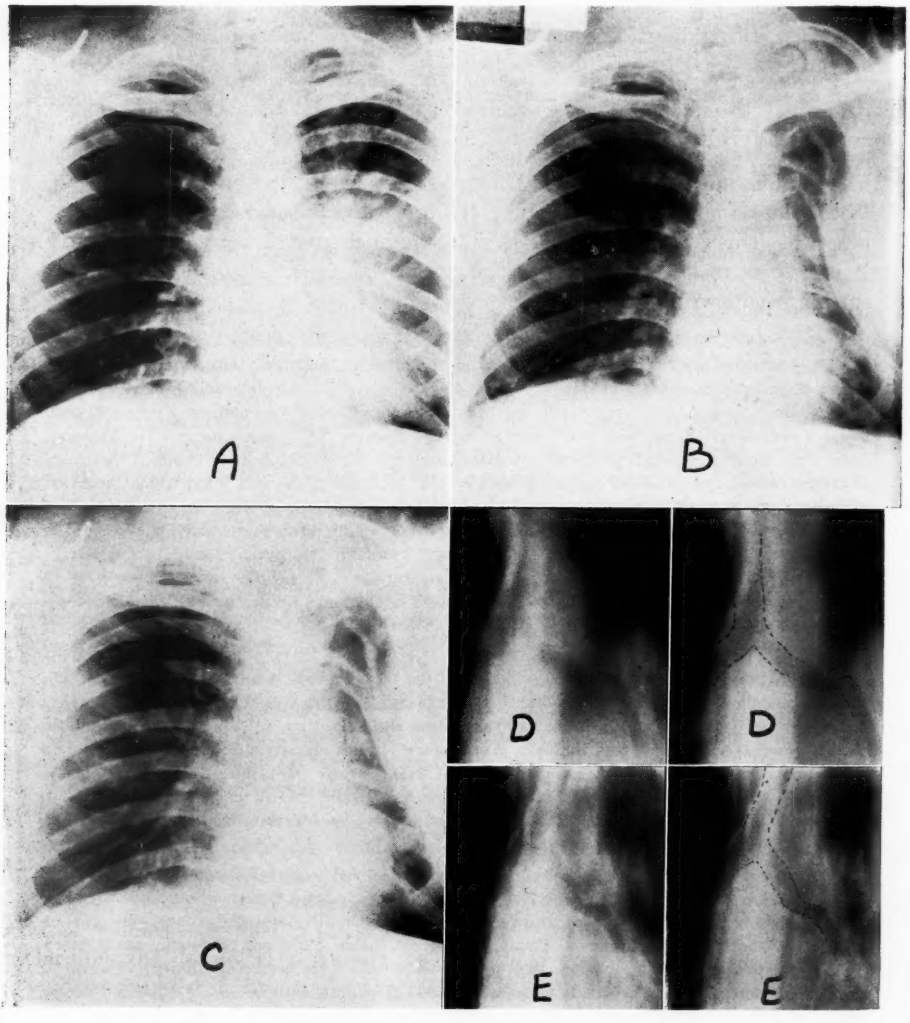

Fig. 4 (Case 8).—*A*, Before operation; extensive infiltration and density left lung, which proved to be entirely confined to the upper lobe at operation. *B*, Three and one-half months after left upper lobectomy, dermal graft of the distal left bronchus, and modified thoracoplasty. *C*, Eleven months after operation; sputum negative; recurrent, tuberculous bronchitis healing. *D*, Marked and unmarked planigrams before operation; severe stenosis of left bronchus in region of upper lobe orifice, which could not be demonstated. *E*, Planigrams eleven months after operation.

The early postoperative course was rather stormy. Good expansion of the lower lobe was slowly gained after the bronchoscopic aspiration of a mucopurulent plug in the grafted bronchus. One month after operation, a 7 by 40 bronchoscope was passed beyond the graft which appeared viable. Two months later it appeared to be covered with epithelium, except for a few, small, irregular, gray areas. The left lower lobe appeared clear in the x-ray film (Fig. 4, *B*). Breath sounds on the left were diminished. The heavily positive, preoperative sputum showed a "rare" bacillus in three of eleven concentrates, during the first three months. Since then, all examinations have been negative, except for one positive culture, six months after operation, which proved resistant to streptomycin. At this time, bronchoscopy revealed a fairly good lumen which admitted a standard 7 by 40 bronchoscope, but there were finely granular, hyperemic, irregular areas, and flecks of gray exudate, evenly distributed over the bronchial surface and the graft. No wire was visible. These findings were regarded as evidence of a recurrent, subacute, tuberculous or mixed infection, and PAS was instituted. Four months later, ten months after operation, there appeared to be satisfactory healing, but PAS is being continued to complete a six month course. There is a small amount of purulent sputum each morning, which contains staphylococci, but no acid-fast bacilli. There are diminished breath sounds at the left base and an occasional wheeze. The patient's general condition is excellent. There is very little cough and much less dyspnea on exertion. The lobectomy and modified thoracoplasty reduced vital capacity to 1,200 c.c., but the tidal air is now 450 c.c., and the ratio 1:2.6. Eleven months after operation, the left lower lobe appeared clear (Fig. 4, *C*), and planigrams showed a fairly good bronchial lumen (Fig. 4, *E*).

Comment.—For the present, this result is considered satisfactory; however, the ultimate result will not be known until sometime after PAS has been discontinued. It is felt that future lobectomy on the left might produce a respiratory cripple, and that such an event would certainly have followed pneumonectomy. In many clinics, no type of surgery would have been offered this case. Certainly, it would not have been intentionally selected for the trial of a new procedure in any clinic.

This experience establishes the fact that, even after careful preoperative study, unexpected operative findings may alter the preoperative intention. This should not be regarded an axiomatic "crutch," but evidence of the failure of preoperative evaluation. Every available means should be used beforehand, to determine whether or not the disease in the lobe or lung distal to the stenosis requires removal, for, at operation, simple inspection and palpation alone are not indicative of the extent or activity of minimal disease. Naturally, advanced or moderate disease is quite detectable, but so is it in preoperative roentgenologic study, and, in such instances, repair of the bronchus would not be contemplated.

In summary, before the possibility of a bronchial graft is considered, the bronchial disease must be regarded as healed, and the lung parenchyma distal to the stenosis considered entirely worth saving—either free of disease, or grossly cleared of previous involvement—without dense scars and healed nodules. A slight degree of bronchial dilatation, especially in the absence of infection, does not, of itself, contraindicate a bronchial graft, but its presence, added to other factors, might do so.

CASE 9.—O. A., woman, aged 50 years. Pulmonary tuberculosis began ten years previously, with positive sputum, cough, wheeze, and minimal pulmonary infiltration by roentgenogram. Left atelectasis and spread occurred in 1942, and acute, ulcerocaseous, tracheo-

Fig. 5 (Case 9).—*A*, Expiration; *B*, inspiration, x-ray films before operation show minimal infiltration just off the left hilus, and marked expiratory block of the left lung. *C*, Ten months after left upper lobectomy and dermal graft of left main bronchus. *D*, Planigrams before operation; severe stenosis proximal left bronchus. *E*, Planigram at time of discharge; stenosis is well corrected, some narrowing at distal end of graft.

bronchitis was observed. A year later, severe stenosis of the proximal left bronchus was present, and the left lung had cleared, except for a residual patch of infiltration lateral to the hilus. Intermittent episodes of left atelectasis continued through 1943 and 1944. The mediastinum gradually shifted to the left. During 1945, the sputum was negative, the lesion in the left lung stable, and the left bronchus healed with a lumen of 3 mm. Lateral x-ray films located the infiltration in the lingula of the upper lobe. Throughout 1946, 1947, and 1948, the patient was observed closely in the out-patient department, and occasionally bronchoscopy was done. The general health was good; motion and breath sounds of the left chest were diminished, and a marked wheeze was audible. Cough was not a prominent symptom, but was usually necessary during the night to relieve tightness in the chest. The sputum continued negative. Re-evaluation, in 1948, decided against pneumonectomy, because of negative sputum, mild symptomatology, and the slight extent of the parenchymal disease (similar to Fig. 5, *B*). A series of bronchoscopic dilatations was advised. These had no appreciable symptomatic effect, and actually reduced the bronchial lumen. Early in 1949, the sputum became positive, and the symptoms increased considerably. Bronchoscopy and examination showed no change. There was no appreciable change in the x-ray films, and expiration-inspiration films showed a marked mediastinal shift (Fig. 5, *A* and *B*). Planigrams demonstrated the severe stenosis of the left bronchus and suggested a similar deformity of the upper lobe bronchus (Fig. 5, *D*). Dermal graft of the left bronchus and upper lobectomy was recommended, and performed on May 18, 1949.

The postoperative course was exceedingly smooth, with complete loss of cough, sputum, and wheeze. A feeling of tightness disappeared. Deep breathing was easier, and the patient was able to sleep through the whole night without coughing. Bronchoscopy, five months after operation, revealed a clean, healed bronchus with a practically normal lumen at the carina. Opposite the former site of the upper lobe bronchus, the lumen was oval in shape and measured approximately 6 by 4 mm. Postoperative planigrams (Fig. 5, *E*) showed a good bronchial lumen and a well-placed wire within the graft. Ten months after operation, she is doing her own housework and the left lower lobe is clear (Fig. 5, *C*). The mediastinum is still displaced to the left.

Comment.—One year before operation, this patient was told that the extent of disease, and the symptoms, did not warrant the removal of a lung. This opinion was not entirely satisfying, but the release from the prospect of a major operation was readily accepted, even on the terms of bronchoscopic dilatations. When the sputum became positive and symptoms increased, this patient, aware of the status of other patients who had received dermal grafts, was anxious to accept surgery. In general, this was an ideal case and a gratifying result.

The lingula of the removed upper lobe consisted of a fibrotic segment with dilated bronchi full of caseous material. The remainder of the lobe exhibited mild dilatation of the bronchi and a few, healed, tuberculous foci. There has been every indication that the lower lobe is practically normal. These findings are considered most unusual in the presence of a severe stenosis for seven years. Ordinarily, lung destruction would have progressed to an advanced state in a much shorter time. Perhaps the absence of significant infection is responsible. At least, the duration of a stenosis is not always an index of the degree of parenchymal damage.

The technical result lacks perfection only because of the oval, somewhat diminished, lumen at the distal end of the graft, somewhat beyond the original stenosis. This is likely to occur if a graft is not extended well into the normal structures above and below the stenosis. Tracheal extension is easy, but dis-

tal extension into the lower lobe bronchus is limited at the orifice of the superior segment, unless the bronchial incision is carried into this bronchus, and the graft inserted as a part of its lumen.

CASE 10.—K. M., woman, aged 49 years. Following hemoptysis, in 1945, this patient was admitted with a history of cough and wheeze for the previous year. Bronchoscopy revealed a moderately severe, healed stenosis of the left bronchus, beyond the carina. The admission roentgenogram is reproduced in Fig. 6, *A*. A marked wheeze was audible on the left. Despite this, pneumoperitoneum was started in October, 1946, and discontinued after one year, because of persistently positive sputum, cough, and wheeze. Shortly thereafter, the sputum became negative and gradual x-ray clearing enused. In June, 1948, an ambulant status was assumed. In less than a year, cough and wheeze increased markedly, and the stenosis was found to have a lumen of 2 mm. in the mid-portion of the left bronchus. The status of the left lung (Fig. 6, *B*) was debatable. Planigrams (Fig. 6, *D*) showed no enlarged bronchi distal to the stenosis. During the previous twenty months, thirty-five three-day sputum concentrates had been negative, except for two questionable bacilli in February, 1949. There was no contraindication to left pneumonectomy, but the left lung was probably stable, and considered worthy of salvage.

At operation, on June 8, 1949, the pleura, including the fissure, was practically free of adhesions. The lower lobe seemed normal, except for some firm, central induration. Multiple, hard, small, discrete nodules were palpable in the upper lobe, most marked near the anterior surface of the lingula. Examination of the opened bronchus showed practically normal lobar orifices, no retained secretions, and a healed, severe stenosis in the distal two-thirds of the main bronchus. A dermal graft was applied to the stenosed bronchus, and no pulmonary resection was performed. Reactivation of the parenchymal disease was considered no more than a possibility. In that event, pneumonectomy could be done later.

On the second postoperative day, bronchoscopic aspiration of a mucous plug from the left bronchus was performed (the only instance, in the series, of bedside bronchoscopy). Thereafter, good aeration of the left lung ensued and persisted (Fig. 6, *C*). This patient no longer has cough, wheeze, sputum, or chest tightness, and feels that she can breathe much easier and deeper. The bronchial graft is completely healed and clean. The bronchus admits a standard 7 by 40 bronchoscope, however, the walls are soft and pliable and the lumen makes a noticeable posterior dip. Planigrams (Fig. 6, *E*) show a much improved airway and a well-placed wire in the graft. Except for one positive culture, six months after operation, all sputum examinations have been negative, as before.

Comment.—This graft was applied in the presence of definite parenchymal disease of uncertain stability, which, at the present time, ten months after operation, is certainly no more active than before operation, and symptomatic relief has been gained without removal of the lung. The one positive sputum culture is suspected to have come from the lingula. Perhaps resection of the upper lobe, at least lingulectomy, at the time of the bronchial graft, would have been better treatment. The answer depends on the future course of the patient. The fact that the operative procedure has not caused regression of the parenchymal disease is considered significant.

FATE OF THE GRAFT

The seventh and eleventh patients were operated upon primarily for severe, tracheal stenosis; both had marked stenosis of the right bronchus, in addition. They have been reported in detail.[2, 3] The latter died, probably because right pneumonectomy was performed at the time of the tracheal graft. The former had separate grafts applied to the trachea and to the right bron-

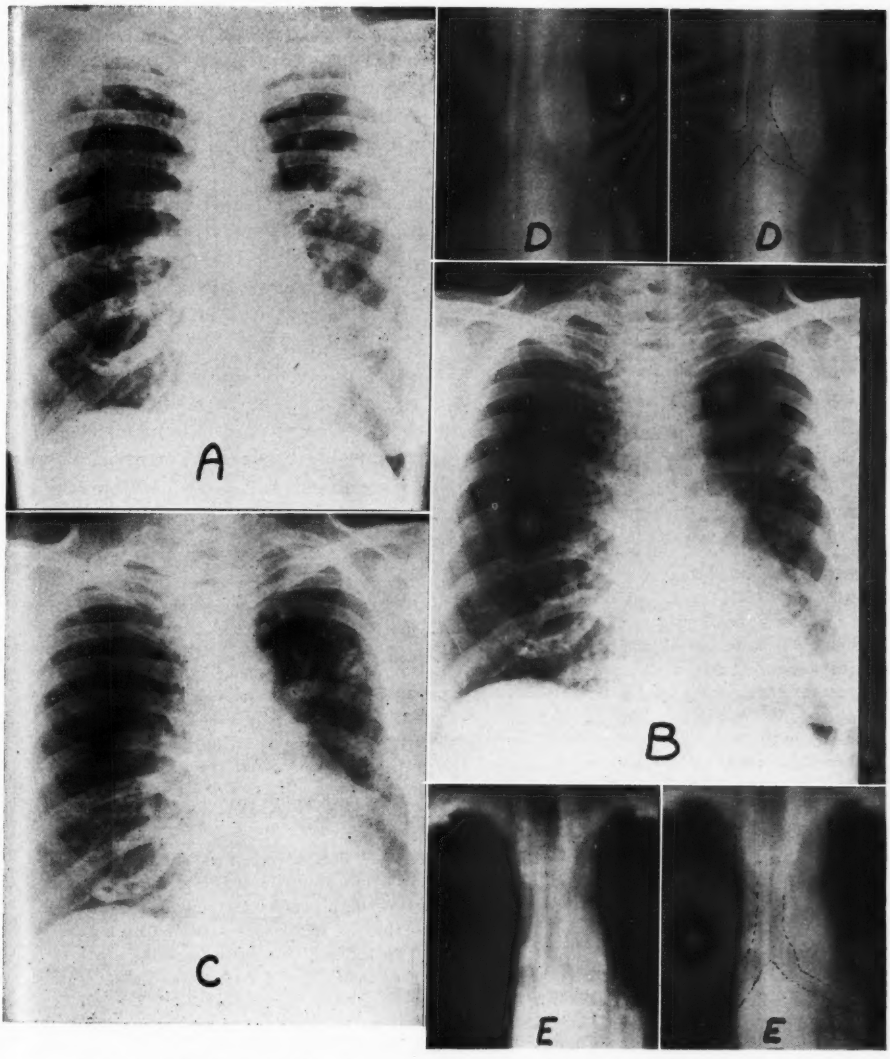

Fig. 6 (Case 10).—*A*, Admission roentgenogram, 1945; scattered infiltration both lung fields, more marked on left. *B*, Four years later: sputum negative, severe obstructive symptoms secondary to stenosis of left bronchus, shown in *D*. *C*, Nine months after dermal graft of left main bronchus: no pulmonary resection. If active disease persists, it probably is located in the left, second, anterior interspace, where the original disease was the most extensive. *D*, Preoperative planigrams, showing stenosis distal half of left bronchus. *E*, Rather poor reproductions of postoperative tomograms which did show a good bronchial lumen. The wire in this graft is perfectly placed. The loops are close together and their shadow is blurred by cardiac motion, during exposure. This diminishes the contrast between the bronchial lumen and the denser surrounding structures.

chus. The tracheal result was excellent; the bronchial graft was functionally adequate, with a lumen approximately one-half normal size. It led to aeration of atelectatic segments, not recognized before operation, which proved to be bronchiectatic, and responsible for symptoms requiring right pneumonectomy almost one year after the dermal grafts had been applied. This patient is now well and convalescing. A previous report[3] of this case contemplated resection, but the operative and microscopic findings have not been recorded.

At the time dermal grafts were first proposed for the reconstruction of stenosed bronchi,[1] the possibility was expressed that a dermal patch might act as a temporary seal of the enlarged bronchus, and supply a scaffold for natural regeneration and healing, rather than survive as a portion of the bronchial wall. Such a process is the only conceivable means of ultimate healing when the graft becomes detached from the bronchus, as in Case 5. Partial destruction of the graft by infection might also stimulate a similar healing effort, even though the graft in Case 6 apparently survived recurrent infection. On the other hand, in the absence of these complications, the evidence of Case 7 indicates the whole dermal patch survives as viable tissue, and becomes a living part of the bronchial wall, over the same area and exact location of its original insertion.

CASE 7.—On February 15, 1950, M. T., man, aged 35 years, had a right pneumonectomy performed, as stated previously, just two weeks short of one year after dermal grafts had been applied to both the trachea and the right bronchus.

The gross findings, at operation, exceeded all expectations. The grafted right bronchus was approached from the posterior aspect; the overlying lung separated easily from its posterior surface; the graft was exactly where it had been placed, most of the fine wire sutures being embedded and invisible. It was yellowish pink in color, and, except for the absence of cartilages, very similar in appearance to the adjacent bronchus. The line of union was indistinct, but discernible because the graft was somewhat thicker than the bronchial wall, and because an occasional tip of a wire loop within the graft, was visible at the margins of the graft, where it joined the bronchus. These short segments of wire were well covered with fibrous tissue. No wire was visible on the surface of the graft, which was smooth and exhibited a slight posterior bulge.

As previously reported,[3] ventilatory studies had demonstrated excellent function in this patient. The preoperative plan was right lower lobectomy, and possibly a wider graft in the right bronchus. The patient was also aware that pneumonectomy might be necessary. In order to inspect the lobar bronchi, and thereby gain more information regarding the necessary extent of resection, the bronchus was opened lengthewise through the graft.

The wire within the graft was completely embedded, and each strand was divided with scissors. The graft cut like skin, and seemed thicker than originally. The cut edge looked like freshly incised skin, with multiple, minute, bleeding points. The whole circumference of the bronchial lumen was smooth, moist, and glistening. It was pale and appeared to be lined with a thin, mucosal layer. From the bronchial lumen, the junction of graft and bronchus could not be identified. The middle and upper lobe orifices were thickened, and the spurs rounded. Each orifice was patent and approximately 5 mm. in diameter. Lower lobectomy was decided upon, with closure of the proximally opened bronchus, or an additional small graft. The opened bronchus was packed with moist gauze to prevent leakage of the anesthetic gases, and seepage of blood into the lobar bronchi and trachea. These structures were aspirated and the packing renewed a number of times during dissection and treatment of the lower lobe hilus. Although the procedure was necessary, it was done reluctantly and carefully, for the thin membrane, lining the bronchus, obviously was being removed.

With the main bronchus open and packed, the right lung was atelectatic, and differential lobar inflation was inapplicable. The lobar fissures were fused. During their difficult separation, the anterior segment bronchus of the upper lobe was inadvertently incised through the point of its division into three branches, where reunion by suture was impractical. Therefore, because of the somewhat questionable status of the middle and lower lobes,[3] pneumonectomy was done, rather than excision of the damaged segment.

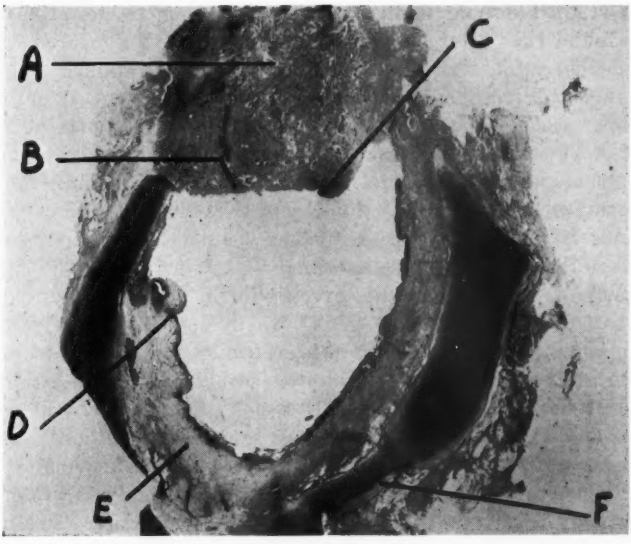

Fig. 7 (Case 7).—Transection of distal, right bronchus, taken near end of graft, approximately one year after original operation. *A*, Dermal graft, posterior wall of bronchus. *B*, Denuded surface toward the bronchial lumen shows no cellular infiltration. *C*, Basophilic granular material suggesting degenerating epithelium. *D*, Atrophic, bronchial epithelium. *E*, Severe fibrosis of bronchial wall. *F*, Healed, or regenerated, cartilage.

The removed lung exhibited no active tuberculous process, bronchiectasis of the middle and lower lobes—not marked in the former—and a small, recurrent, subpleural cyst in the upper lobe, plus fibrosis. Microscopic sections of the grafted bronchus (Fig. 7) disclosed bronchial fibrosis without absolute evidence of tuberculosis. On the side of the bronchial lumen, the dermal graft had no epithelial covering, and the absence of surface, cellular infiltration indicated that something had been removed. In some sections there were folds and recesses of the dermal surface. In these areas, a granular, basophilic material covered the derma. It could not be identified, but suggested degenerated, nuclear fragments, possibly residual, squamous epithelium. In isolated areas, remnants of a bronchial type of epithelium were encountered which may have been displaced from the dermal surface. In a few, small fields, simple, cuboidal epithelium covered the derma.

In one longitudinal section, near the junction of the graft and bronchus, an island of growing cartilage was observed, possibly representing regeneration of cartilage toward the graft, if not into it.

Dr. I. L. Tilden, consultant pathologist, made special stains and studied the sections. A portion of his description follows: "The dermal graft, itself, was composed of normal-appearing, collagen bundles, containing several groups of sweat glands, and in one preparation, a pilo-sebaceous apparatus was present. The sweat glands were lined by well-preserved epithelium and appeared entirely normal. Verhoeff's stain showed a normal elastic tissue pattern, and various collagen stains showed no deviation from normal on the part of the collagen bundles, except a tendency toward hyalinization in isolated areas."

Apparently a dermal patch, sutured into a bronchial defect, with one surface exposed to the air passage, survives, with little change in its elastic and collagen elements.

Concerning the preservation of these elements, viability of the graft, and the disappearance of sebaceous and hair-follicle structures, the findings in the preceding case are the same as the histologic observations of Peer and Paddock,[5] who studied dermal implants in subcutaneous tissue. On the other hand, they found that after one year, the sweat glands appeared to be in a process of degeneration and replacement. In addition, retained fragments of epidermis survived long, and produced microscopic, cystic structures, and granulomatous areas. In the preceding case, the sweat glands do not show such changes, but appear diminished in number, and the only suggestion of epidermal structures are occasional areas of granular, basophilic material on the dermal surface. Also, the distribution of the collagen bundles and elastic tissue strands is practically normal. They do not appear contracted, and coiled up, as in the case of implanted derma.

Despite the scarcity of dermal covering in the sections studied, it is felt that some sort of epithelium existed that was removed during the operation. In other patients, the bronchoscopic appearance of grafts suggests an epithelial covering after a few weeks, which later becomes grossly indistinguishable from adjacent bronchial epithelium. It is felt that the removal of a good thickness of epidermis, at the time the graft is made, encourages an ingrowth of bronchial epithelium, and that residual areas of squamous epithelium eventually degenerate. If considerable squamous epidermis is present on the graft, it is likely to survive as such, at least, for some time. This is not entirely objectionable; however, ciliated bronchial epithelium would be ideal. Perhaps with the passage of more time, such favorable changes will occur.

It seems illogical to expect more normal epithelium than that which covers a healed stenosis. Nevertheless, studies of such bronchi in surgical specimens usually reveal a thin, loosely attached, atrophic type of bronchial epithelium, and a scarcity of mucous glands. Frequently the epithelium covers dense, avascular, scar tissue, which appears much less suitable as an epithelial base than a viable dermal graft.

Regardless of the ultimate type of epithelium covering a dermal graft, the absence of cilia should not be an objection to the procedure, for the graft only increases the bronchial circumference; it does not change or remove the epithelium which previously lined the bronchus, and ciliary action over a part of the bronchial circumferences should persist.

CONCLUSIONS

Until a better method is discovered, the judicious use of wire-enforced dermal grafts for the reconstruction of tuberculous tracheobronchial defects will salvage healed or disease-free lung tissue, destined for destruction by such defects. At the present time, there is a significant need for such a procedure in the treatment of tuberculosis. This need may be diminished by modern treatment, but it is likely to continue for some time. In addition, the

method should be considered in the treatment of other tracheobronchial defects, for it is regarded as superior to the use of fascia, foreign body tubes, tantalum gauze, and other substances. In all probability, a more general use of wire-enforced dermal grafts will lead to an improved method, or the discovery of a better procedure.

Histologic and anatomic evidences, plus clinical results to date, indicate that dermal skin actually fulfils all the proposed requirements of bronchial grafts enumerated in a previous publication,[1] and survives as a highly suitable portion of the bronchial wall. Ultimately good clinical results may be obtained, despite the occurrence of complications, such as partial separation of the graft from the bronchus, and recurrent tuberculous infection.

The success of tracheobronchial dermal grafts depends on many factors, as illustrated by the reported cases. They include numerous features of operative technique and judgment, careful preoperative evaluation of the tracheobronchial defect and the parenchymal disease in each lobe, the application of resection whenever indicated, and the avoidance of its substitution by a dermal graft. Other factors are a meticulous preparation of the graft, the use of fine wire for its framework and sutures, abstention of tension caused by grafts of too much width, extension of the graft beyond the stenotic area, and the precise use of antibiotics before, during, and after operation. The use of early ambulation, physiotherapy to promote lung expansion, and the maintenance of an adequate airway are important postoperative measures, as well as the preservation of fluid, blood, and nutritive balance.

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DISCUSSION ON "THE EXPERIMENTAL USE OF HOMOGENOUS TRACHEAL TRANSPLANTS IN THE RESTORATION OF CONTINUITY OF THE TRACHEOBRONCHIAL TREE" BY DR. TRUXTON L. JACKSON, DR. E. J. O'BRIEN, DR. WILLIAM TUTTLE, AND DR. JOHN MEYER;* "RESECTION OF THE TRACHEA AND BRONCHI" BY DR. MAX G. CARTER AND DR. JOHN W. STRIEDER;† AND "FURTHER EXPERIENCES WITH DERMAL GRAFTS FOR HEALED TUBERCULOUS STENOSES OF THE BRONCHI AND TRACHEA" BY DR. PAUL W. GEBAUER

DR. ANDRE JUVENELLE, Paris, France.—I should like to thank The Association for the privilege of discussing the valuable contributions of Dr. Jackson, Dr. Carter, and Dr. Gebauer and their co-workers. I must also express my gratitude to Dr. John D.

*See page 598 for article by Jackson, O'Brien, Tuttle, and Meyer.
†See page 613 for article by Carter and Strieder.

Stewart, who has made it possible for me to work this year in his department at the University of Buffalo Medical School, with the constant collaboration of Dr. Coleman Citret. Our work has been along similar lines. I have enjoyed these papers very much, and it is now with a feeling of how small and inadequate our knowledge is on this subject compared with the large experience of the speakers that I would like to make the following remarks.

When Dr. Citret and I became interested in this field of investigation we were unfortunately not aware of Dr. Jackson's work published in October, 1949, in THE JOURNAL and our approach to the problem has been somewhat different from his. Our first experiments consisted of severing the right or left main bronchus, closure of the proximal bronchial stump, and reimplantation of the bronchus 2 or 3 cm. higher in the trachea through a window cut in the tracheal wall. After several failures due to difficulties with the anesthetic technique we succeeded in carrying out the procedure on five successive dogs, all of which had uneventful recoveries.

(Slides.) These slides illustrate the essential features of the anastomosis. The dogs were not given any antibiotics. They were followed by fluoroscopic and bronchoscopic examination at various intervals. It is naturally too soon to draw final conclusions, but the animals apparently show good healing and pulmonary function. The longest follow-up at present is four months. We are well aware that by this technique the tracheobronchial anastomosis was effected by sutures under considerable tension. This was deliberate, since it was felt that (1) conditions encountered in patients might necessitate removal of tissue and creation of defects which would have to be closed with some degree of tension unless prostheses or grafts were to be considered; and (2) this method was also used as a trial technique in preparation for attempts at resection of the entire tracheal bifurcation and reconstruction without prosthesis.

Our next experiments attacked this problem. The distal three or four rings of tracheal cartilage, along with the entire right main bronchus and similar length of left main bronchus was resected. Reconstruction was done by performing an end-to-end anastomosis of the distal end of the trachea and one of the main bronchi, then reimplanting the other main bronchus higher on the trachea, as described in the previous experiment. Two main obstacles were encountered: (1) adequate anesthetic apparatus and methods to maintain oxygenation throughout the procedure (the solution of these difficulties will be reported at a later date); and (2) tension at the suture lines due to the large defect. Attempts were made to elongate the trachea by making opposing partial circumferential incisions and covering the defects with fascia lata grafts. In our hands this method did not prove feasible. Then, somewhat to our surprise, we found that by freeing the trachea superiorly from its surrounding tissues in the mediastinum, it was possible by simple downward traction to bridge the defect and carry out the anastomoses.

(Slides.) These slides illustrate the resection and anastomosis. The procedure has been carried out on six dogs to the present time. Four have survived and are apparently well. One death on the ninth postoperative day showed good healing of the anastomoses at autopsy, the cause of death being distemper which was rampant in our kennel at that time. The sixth dog, which died on the third postoperative day, died during attempted functional studies. In carrying out these experiments pulmonary functional studies with the bronchospirometer and chemically induced bronchospasm have been done both pre- and postoperatively. Time does not allow a discussion of the results of these studies.

In conclusion, I have found the papers given today to be of great interest because I feel that a combination of grafts and transplants together may furnish answers to many unsolved problems in this field.

DR. ORLAND DAVIES, San Francisco.—During the past year, work has been in progress in the experimental surgery laboratories at the University of California School of Medicine, on homologous tracheal grafting in dogs. Sampling experiments were done with eleven animals to test the efficacy of various methods of preservation of tracheal grafts.

Although tracheal grafting procedures done without internal support were well tolerated in the immediate postoperative period, stenosis at the site of grafting occurred in all instances regardless of the method of preservation of the graft.

A technique was then developed whereby stenosis at the site of grafting was avoided by the use of a plastic (acrylic) tube used as an internal support for the tracheal graft. This procedure was used successfully to place grafts in the cervical and thoracic trachea in fourteen animals. These animals have remained free of respiratory difficulty two to six months after tracheal grafting. A similar method has been used to bridge defects formed by removing the distal trachea, carina, right lung, and a portion of the left main bronchus. Two animals in which the latter procedure was done have survived for two weeks and six weeks following the pneumonectomy and tracheal grafting procedure. This work will be completed and submitted for publication in the near future.

DR. F. J. JARVIS, Seattle.—I should like briefly to further the discussion of these excellent papers by presenting an attempt at replacement of the mediastinal trachea in man. In the first slide we will see a tracheogram of a man aged 33 years, who presented himself to me three days before I left for the St. Louis meeting of this Association, having had for twenty-two months symptoms of cylindroma of the trachea, and for eighteen months had had, on three occasions, endoscopic fulguration down to beneath the mucosal level.

(Slide.) In the tracheogram you will see the defect, representing the tumor which endoscopically appeared to be obstructing the trachea for about two-thirds of its lumen. The man was incapacitated almost wholly by the tracheal obstruction. I was stimulated by Dr. Daniel's report at that time, and also by a slap on the back from Dr. Berry, to return and attempt to excise the lesion.

(Slide.) You see here the artist's conception of the method used; the sternal splitting incision. The trachea was dissected free and 4 cm. of the trachea were removed and the trachea was replaced by a stainless steel tube. We selected stainless steel because of the difficulty in the wilds of Seattle of obtaining a Vitallium tube, and also its expense—when one considers that I had to make up several tubes not knowing which one I would use. This is a very simple tube and proved to be in this case at least temporarily satisfactory.

(Slide.) One sees here the tumor. You will observe that the tumor is obstructing the trachea markedly. It is a cylindroma although it has totally destroyed the wall and is invading the surrounding structures, but at this time it has not metastasized. I should prefer to call it an adenocarcinoma Grade 1, rather than a cylindroma which, as we know, is a metastasizing tumor, although metastasis occurs rather late.

(Slide.) You see the film taken on the tenth postoperative day, two days before the patient left the hospital. The tracheotomy was life-saving in his case, in order to evacuate secretions. He was gradually able to overcome this difficulty, and the tracheotomy was removed immediately after this film was taken and he left the hospital.

(Slide.) This film was taken a year later, with the tube still in place. The man has been working during this period, the operation having been performed in June, 1947. At this time the patient was perfectly well, and then I made my fatal error. Relying upon the previous experiments as related by Dr. Daniel, in which a rigid trachea was shown in dogs to have been regenerated surrounding these tubes, I removed the tube. The trachea that had been regenerated was sufficient to handle this patient for three weeks, but it was not because of stenosis that I was forced to replace the tube, it was because the patient, during cough, had not a sufficiently rigid trachea to handle it. He handled quiet inspiration and quiet expiration quite satisfactorily.

(Slide.) This is the tube which has not been cleansed, which has been in the trachea for thirteen months. Unfortunately, I do not have the slide which shows the lumen of the tube. It looks as if it had been taken out and scrubbed daily. The cough reflex was sufficient to keep it clean.

The unfortunate thing is that within three weeks I had to replace this tube and at that time there was a shadow in the upper right pleural cavity; there was also an adenoma of the left bronchus. Shortly, the patient began to show metastases.

I have unfortunately not the slide showing the autopsy specimen thirty-three months after the initial operation, in which there was generalized pulmonary and pleural metastases. Suffice it to say that in this one case the method seemed to be adequate, and had I left the tube in I am sure the patient would have been comfortable for a much longer time.

DR. W. E. BURNETT, Philadelphia.—I hesitate to prolong this discussion, yet these excellent papers are so stimulating that I want to present briefly some information we have obtained in the laboratory in the last two years. Dr. Robert M. Bucher and Dr. George P. Rosemond have done most of this work. We wanted to get something that would be easily accessible, that would be cheap, that would have rigidity enough to be molded, that would have a benign influence on the surrounding tissues, and therefore chose stainless steel wire mesh and performed some experiments on these dogs.

(Slide.) First, the tracheal ones, in which between four and six cartilages were removed, of the complete circumference after the first one in which partial circumference was utilized; the wire mesh was then placed overlapping the unopposed ends and sutured to the trachea with wire sutures. These two examples were sacrificed after five and six months, showing a considerable amount of epithelization, though still some granulations persisting, showing a good lumen with no evidence of stenosis. Unfortunately, they were not very carefully supervised, and we found that the animal house man had decided not to vaccinate against distemper, which had been our habit, so we lost two of these from distemper, one from massive infection, and one from too much anesthesia, out of ten dogs. However, those that survived the immediate period had an uneventful course until sacrificed.

(Slide.) It was difficult to make sections of these sacrificed specimens because of the incorporated wire, but by peeling off some tissue one can see that there is some degree of regeneration of cartilage as well as the lining membrane.

(Slide.) In the thoracic trachea, additional attempts were made but the mortality was quite high because of the same errors which I mentioned, plus inadequate amounts of antibiotics or attempts at mechanical removal of air in the chest due to leakage which occurred after a matter of three to five days, although skin grafts and pericardial grafts were used to reinforce the wire mesh which was the basis. Here is an example of a specimen four and one-half months after survival and sacrifice, in which one can see some of the wire mesh showing through by transillumination, although it has a slight covering of epithelium; it is infiltrated with tissue and was airtight. This dog had only a partial defect, as you see, rather than a complete circumferential one. Good regeneration of cartilaginous rings is demonstrated.

(Slide.) This is another slide of the inside, showing the wire mesh infiltrated by tissue but with incomplete covering; the edges, however, are well epithelized after about three months.

(Slide.) This is the outside view of the same specimen. This method gives promise and warrants further investigation. We are continuing the study.

DR. C. L. HOLMES, Boise, Idaho.—I, too, am reluctant to prolong this discussion but I think it is appropriate at this time to report a clinical case. About July 4, 1949, a man was taking off in his privately owned plane and crashed, and apparently received some injury to the midcervical region. He was admitted to the hospital several hours later, complaining of pain in the neck, some shortness of breath, and after a little time became cyanotic and apneic. An emergency tracheotomy was done by his local doctor and resuscitation was effected. Ten days later, the doctor opened his neck, explored this region, and found three cartilagenous rings crushed. These were removed in toto and an end-to-end anastomosis was effected with silver wire. A proximal tracheotomy was added through this area and ten days later the tracheotomy tube was removed. The stenosis was prompt, the patient was in considerable difficulty and the doctor could not reinsert the tracheotomy

tube, and I was called. A dilatation through the tracheotomy wound was effected and the tube was reinserted. This was left for three months, then removed, and after a week or so the trachea began to stenose again, the patient was having dyspnea with exercise, and was raising considerable amounts of mucus. Being familiar with Dr. Jarvis' case, and the work of Dr. Clagett and Dr. Grindlay, I felt that some type of prosthesis should be used. A Vitallium tube three-fourth inch in length was constructed with a flange at each end with multiple perforations around it, and the stricture was dissected out and removed completely. Each end of the trachea was then sutured directly to the end of the tube. This was quite effective in relieving the patient, but about a month later he again noticed that he had difficulty in raising mucus. Bronchoscopy was done, a 9 mm. bronchoscope was dropped through the area without any difficulty, there was no stricturing tendency, but there seemed rather to be redundancy of mucosa at each end of the trachea. Dilatations were done periodically with the bronchoscope every one to two weeks for two or three months.

A month ago we went back into the neck and removed the original Vitallium tube and reinserted a one and one-eighth inch stainless steel tube completely within the trachea, projecting ½ to 1 cm. into the cricoid ring and into the distal trachea. On bronchoscopy just before leaving for this meeting, there was a complete airway, complete freedom of respiration with exercise, and we hope this will be effective in relieving him permanently. However, I felt that perhaps that was true with the first tube.

DR. STRIEDER (closing).—Many of you are familiar with Rob and Bateman's article in the October, 1949, *British Journal of Surgery*, in which they described the use of tantalum gauze covered with fascia to effect a repair of the cervical trachea. Their partial tracheal resection was for a recurrent carcinoma of the thyroid and included about six rings and the cricoid cartilage. They bridged the tracheal defect with tantalum gauze covered with fascia. Their difficulty was that they noted inspiratory stridor due to flutter of the free lining of the tantalum gauze tube, and overcame it by fulgurating the lining to create point adhesions. In our laboratory experiments we noted a similar difficulty and overcame it preoperatively by using interrupted sutures to fix the lining to the gauze. They also noticed emphysema in the neck and I presume, although the discussors did not mention it, that it was a complication of some of these repairs of cervical tracheal defects. The difficulty with tantalum gauze, in our experience, is that unless there is left a narrow rim of the posterior tracheal wall for suture purposes, obtaining an airtight closure posteriorly is almost impossible. In the thoracic trachea this would, and did in our cases, result in tension pneumothorax.

It is our impression that repair of the cervical trachea is easier than the thoracic trachea for reasons that have been stated by the discussors, and also because of the contiguous structures that buttress the suture line and tend to seal it more effectively.

THE TECHNIQUE OF PULMONARY DECORTICATION AND PLEUROLYSIS

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INTRODUCTION

THE recent war revived interest in the operation of pulmonary decortication and firmly established its value in the treatment of clotted hemothorax and its complications.[1-6] Impressive results in new applications[7-15] of the procedure have rapidly followed the military experience. In the numerous articles that are currently appearing in the literature, the matter of operative technique is given, for the most part, only passing consideration. The purpose of this article is to consider this phase of the subject and to emphasize the importance of pleural adhesions in the production of the pulmonary collapse. A modification of the usual operative technique will be described which has been used during the past two years in a group of patients requiring decortication for a variety of indications. This technique has substantially reduced the time required for the operation, the blood loss, and more importantly, has minimized injury to the lung.

GENERAL CONSIDERATIONS

It is not the intent of this article to consider the etiology, the various indications for operation, or to discuss the factors inherent in the collapsed lung[16, 17] which influence the operative result. We are concerned here entirely with operative technique and benefits that can be anticipated in patients properly selected for this procedure. Regarding this entire group, several generalizations can be made. The lung is maintained in its collapsed state by (1) the contents of the pleural space (air, blood clot, fibrin, fluid, or pus), (2) the peel, (3) pleural adhesions between the lung, chest wall, pericardium, diaphragm, and mediastinum.

Each of these factors is not equally important in maintaining the lung in its collapsed state. In the development of the pathology, collapse of the lung by hemothorax or pneumothorax occurs first, following which the peel and pleural adhesions develop simultaneously. For practical purposes, centripetal collapse never occurs, the lung being merely compressed toward the mediastinum (Fig. 1). The pleural adhesions thus form after various degrees of pulmonary collapse have already occurred. Their role in the pathology is directly pro-

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portional to the degree of compression and for this reason, division of these adhesions becomes an increasingly important part of operative treatment in those having extensive pulmonary collapse.

The peel maintains collapse in a different way. It is approximately the same in size in those patients having comparatively small as well as those having more extensive degrees of pulmonary compression. The importance of its role in maintaining the collapse appears to be directly proportional to the area of the lung which it covers and is inversely proportional to the degree of pulmonary collapse. In short, it appears correct to state that the lung is compressed by the pleural contents, it is imprisoned by the peel, and restrained by the pleural adhesions. This concept of the surgical pathology, as will be shown later, has important practical application in operative treatment.

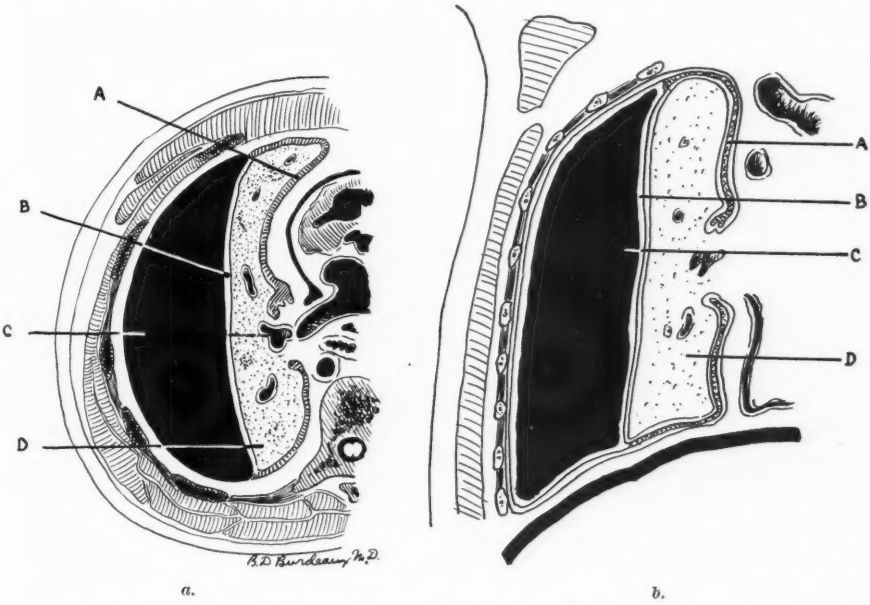
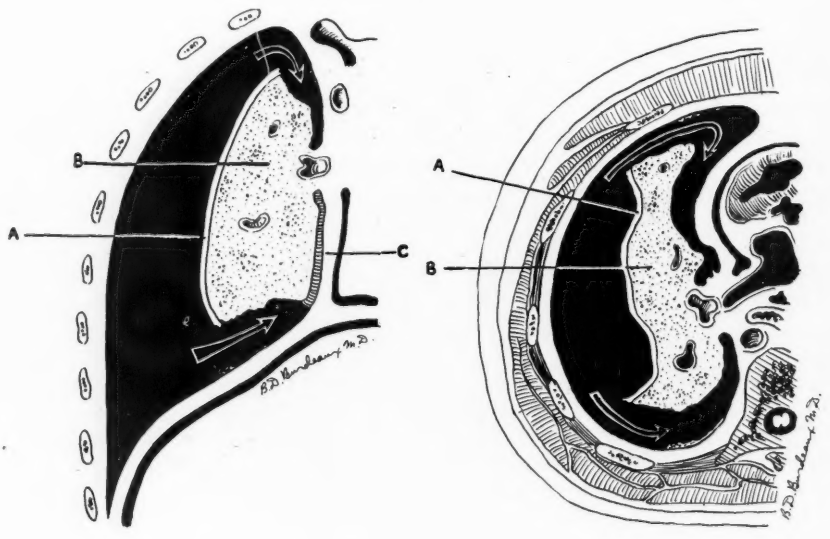


Fig. 1.—Compression of the lung toward the mediastinum is illustrated in cross section (*a*) and coronal section (*b*). Pleural adhesions (*A*); peel (*B*); pleural space (*C*); compressed lung (*D*).

Granted that the lung is capable of expanding, a properly executed decortication is followed by a brilliant operative result in a high percentage of cases. Instances of partial successes and failures in important percentages are included, however, in the results of all who have had extensive experience with this procedure. Injury to the lung producing persistent alveolar leakage and delayed or incomplete expansion is the most important cause of such failures. Lung injury is especially likely to occur if blunt dissection is used to remove the peel of tuberculous patients having a postpneumothorax unexpandable lung. It is in this group that the technique to be described is especially advantageous.

OPERATIVE TECHNIQUE

With few exceptions,[8-11] the operative technique of Sampson and Burford[2] is currently being rather closely followed by others performing pulmonary decortication. This operation requires that the pleural contents, if present, be evacuated initially following which the peel is removed by blunt dissection. As the final step of the procedure, the lung is mobilized by dividing the pleural adhesions. Emphasis is placed on removal of the peel; and the matter of finding the proper plane of cleavage, control of bleeding, and repair of injuries of the lung is given detailed consideration. They discuss pleurolysis briefly and stress that it is an essential part of the procedure. Its importance as compared with removal of the peel is not considered.



a. *b.*

Fig. 2.—The step of pleurolysis is illustrated in coronal section (*a*) and cross section (*b*). The visceral peel has been divided at its periphery and the lung is being fully mobilized. In (*b*) all the adhesions have been divided and the lung is ready for inflation and decortication. This dissection is identical to that which would be required if pneumonectomy was to be performed.

The operation suggested here emphasizes the step of pleurolysis. It differs little from the preceding one except in the order of procedure and method of removal of the peel. The chest is opened using a thoracotomy appropriate for lower lobe lobectomy; this permits a better exposure of the diaphragmatic adhesions which are usually denser than those encountered elsewhere. Pleural contents, if present, are thoroughly evacuated. As the next step of the operation, the visceral peel is everywhere divided at its periphery. Complete pleurolysis is then performed, mobilizing the lung from the diaphragm, pericardium, chest wall, and mediastinum (Fig. 2). This has invariably proceeded readily

with minimal bleeding and usually without injury to the lung, and can often be accomplished for the most part by manual dissection. When pleurolysis has been completed, the anesthetist is asked to inflate the lung. The degree of inflation that is possible at this point is usually surprisingly complete. Not infrequently, the lung can be inflated sufficiently almost to fill the pleural space with the peel still in place. The latter, moreover, shrinks considerably,* and appears to contract to approximately one-half its original size. The lung now being completely mobilized, the lower margin of the shrunken peel is elevated

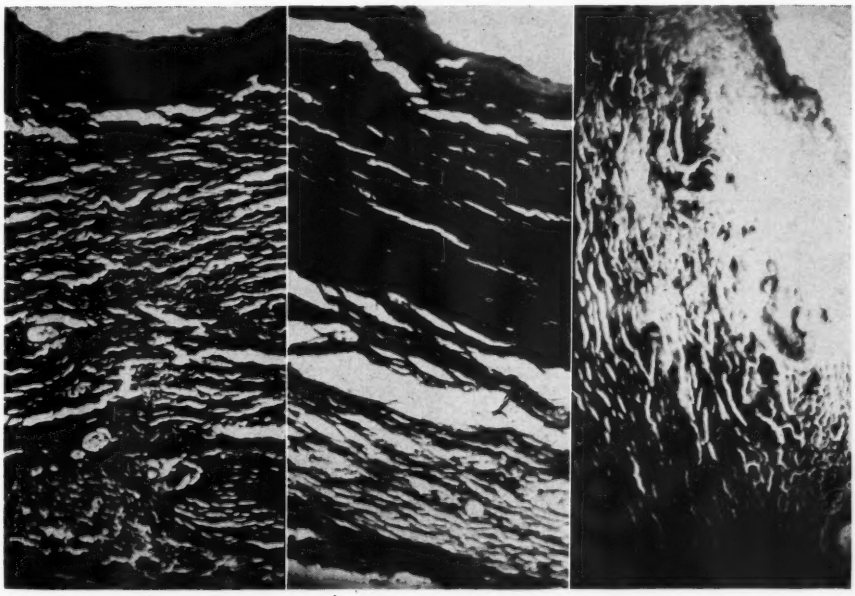


Fig. 3.—Photomicrographs of the peel of three patients is illustrated. The tissue was stained using the Verhoeff technique and was reported† as follows: "The sections disclose many of the individual fibers and masses of the collagenous tissue to stain black indicating presence of elastic tissue. Amounts of elastic tissue vary considerably from one area to another and from one section to another but in general it can be stated that the elastic tissue is quite abundant."

with clamps permitting the operator to develop a plane of cleavage between the peel and the lung in a vertical, rather than a horizontal plane. This enormously facilitates removal which is done using sharp dissection, alternating at times with the gauze covered finger as commonly practiced in isolating the sac of an inguinal hernia (Fig. 4). The laborious use of Küttner dissectors is entirely eliminated and the peel can usually be removed in a few minutes with almost no bleeding or injury to the lung. Performed in this manner, the removal of the peel actually becomes the least difficult part of the operation.

*Shrinkage of the peel has occurred in patients having clotted hemothorax as well as in those having a postpneumothorax unexpandable lung. In the latter group, elastic tissue has been present in the peel in each instance (Fig. 3).

†Dr. Alexander A. Kosinski, Pathologist, C. S. Wilson Memorial Hospital.

The fissures of the lung are opened and the diaphragmatic adhesions are divided as is suggested in other publications. The removal of the parietal peel by dissection has not been done. An anterior and a posterior catheter connected with a subaqueous deflation system has been used to drain the pleural

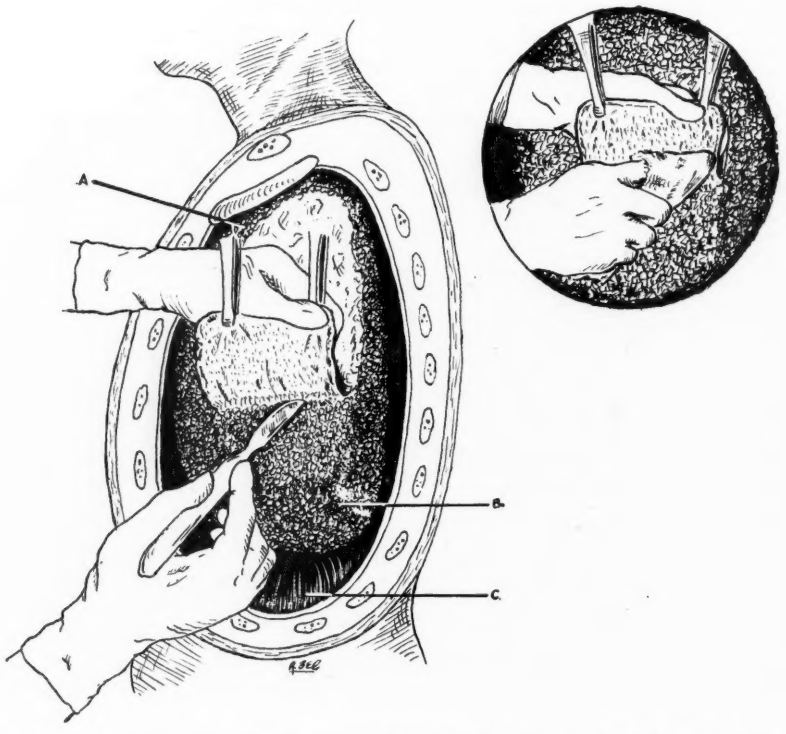


Fig. 4.—The manner in which the peel is elevated and removed is illustrated. Traction permits individual fine fibrous strands between the peel and the visceral pleura to be visualized and divided by sharp dissection. To avoid injury, the operator's attention should be focused on the lung and the knife should be applied to the peel. In this manner the lung is separated from the peel rather than the peel from the lung. The fibrous strands are avascular in instanecs of unexpandable artificial pneumothorax. The insert demonstrates dissection by the gauze covered finger which can be utilized when the peel separates readily.

space. With one exception, which will be referred to later, minimal drainage and prompt re-expansion of the lung has followed permitting their withdrawal within forty-eight hours. In those having tuberculosis, streptomycin, 1 Gm. daily, has been administered for one week preoperatively and continued in similar dosage for two weeks after operation. All patients have received adequate doses of penicillin during the immediate postoperative period.

In decortications performed on tuberculous patients having pneumothorax and an unexpandable lung, a factor of safety may be added by leaving the peel in place over the area which was originally the site of parenchymal disease.[18]

In such patients, additional filling of the pleural space by the lower lobe can often be obtained by dividing the pulmonary ligament.

The following case reports illustrate several features considered in the foregoing; in each instance, intratracheal ether-oxygen anesthesia was administered; the patient was placed in the lateral position and cotton suture material was used throughout.

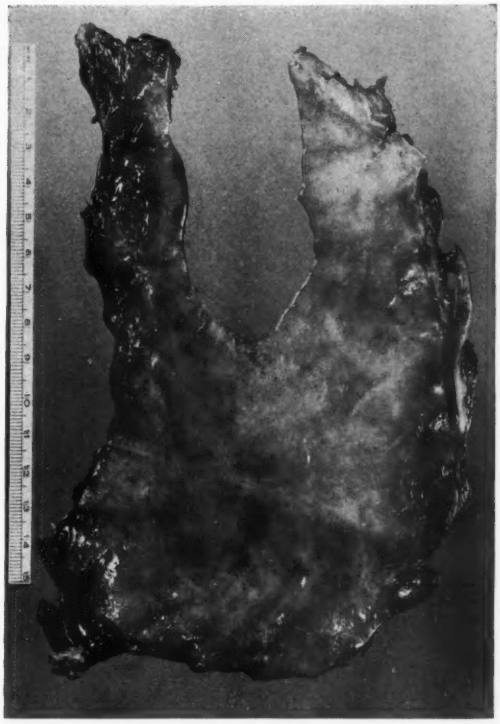
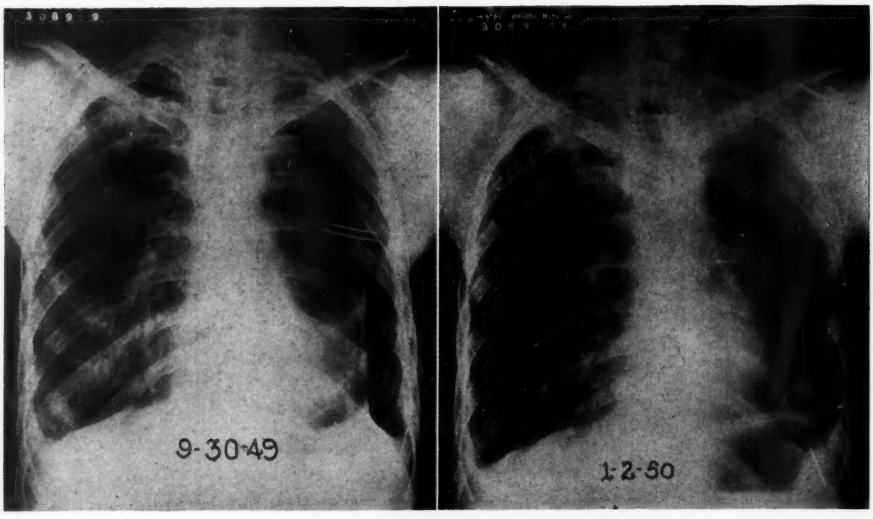


Fig. 5.—A photograph of the entire visceral peel removed from this patient is illustrated. The notch at the upper end is the area where a section of the peel was allowed to remain adherent to the lung. This comparatively small peel covered the entire lung which was compressed against the mediastinum.

CASE 1.—C. G., a 23-year-old white man, had an artificial pneumothorax induced on Sept. 16, 1941, for caseous pneumonic tuberculosis of the upper lobe of the left lung. The patient also had disease in the upper lobe of the right lung without cavitation. Pleural adhesions were present and a closed pneumonolysis was done Nov. 28, 1941. Cavity closure and sputum conversion followed; he had pleural fluid on numerous occasions but never developed empyema. Attempts to expand the left lung were made during 1949, without success. Decortication by the technique described previously was performed on Oct. 24, 1949. After performing complete pleurolysis, inflation of the lung sufficient to obliterate more than one-half the pleural space was possible, with the shrunken visceral peel still in place. The latter was mobilized from below upward, and a portion of it was allowed

to remain over the site of the disease in the left upper lobe (Fig. 5). The pulmonary ligament was divided; the fissures and diaphragmatic sinuses were opened, and the pleural space was drained with two catheters.

The postoperative course was uneventful; re-expansion of the lung was complete in thirty-six hours, at which time the catheters were removed. The wound healed by primary union and the patient was transferred back to another hospital* on the sixth postoperative day. Roentgenograms illustrating the preoperative status and the postoperative result are shown in Fig. 6.



a *b*.

Fig. 6. (Case 1).—The preoperative roentgenogram (*a*) and postoperative study (*b*) are illustrated.

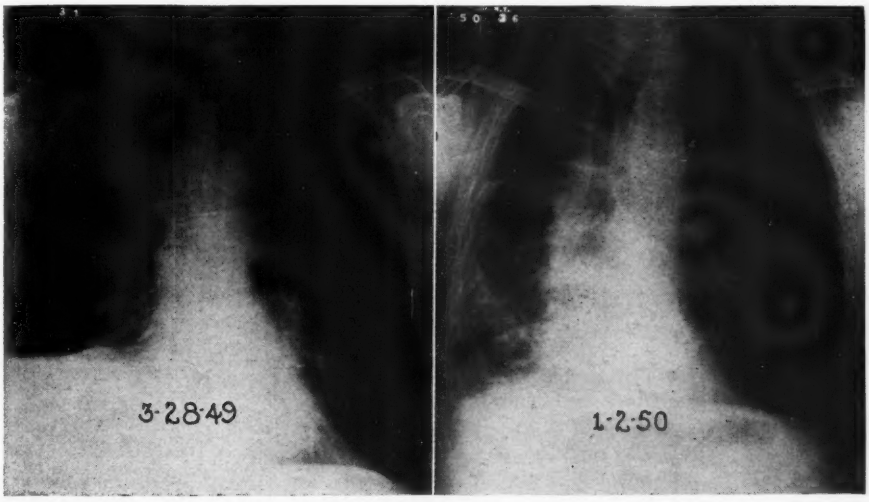
CASE 2.—The following patient is of interest because the improvement which followed operation was due almost entirely to pleurolysis alone. This patient is an example of the type in which pulmonary fibrosis makes complete expansion impossible.

S. W., a 46-year-old man, originally had a large tuberculous cavity in the upper lobe of the right lung, which measured 5 cm. in diameter. Artificial pneumothorax was induced on April 1, 1940. Pleural adhesions were present, and a "difficult" pneumonolysis using enucleation technique was done on June 4, 1940. The cavity then developed tension characteristics, but nevertheless, closed six months later. Density persisted in the area formerly occupied by the cavity, and was believed to be due to inspissated secretions in the latter. The patient's sputum was converted; the pneumothorax was unexpandable. The patient stoutly refused thoracoplasty but accepted decortication. The operation was undertaken with some misgivings because of the size of the original cavity.

At operation, April 5, 1949, the peel was divided at its periphery and the lung mobilized. Re-expansion of the lower lobe was fairly good, and this was improved by division of the inferior pulmonary ligament. A large boggy area, roughly the size of the original cavity, could be palpated in the upper lobe. A similar area was present in the apical segment of the lower lobe. Because of these findings, it seemed unsafe to remove

*Broome County Tuberculosis Hospital, Chenango Bridge, N. Y.

more than a narrow strip of the peel at its periphery, 2.5 cm. in width. A limited thoracoplasty would have been sufficient to obliterate the pleural space, but this was not done because permission for such a procedure had been refused. Following operation, considerable re-expansion has occurred but a small pneumothorax pocket persists. The patient's exercise tolerance has been greatly improved by the operation; he refuses additional surgery. His pre- and postoperative roentgenograms are illustrated in Fig. 7.



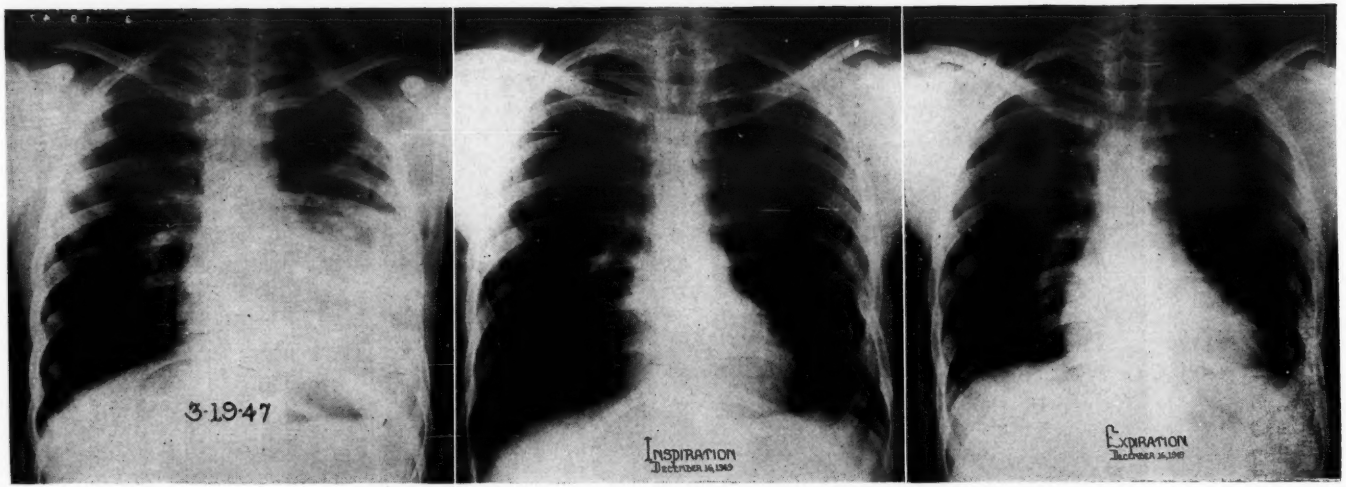
a. *b.*

Fig. 7 (Case 2).—The preoperative roentgenogram (*a*) and postoperative exposure (*b*) are illustrated. Mediastinal displacement has occurred following operation. This patient's exercise tolerance has been more than doubled since decortication.

CASE 3.—This patient is believed to be an example of so-called idiopathic spontaneous pneumothorax in which a torn vascular adhesion produced a simultaneous massive hemothorax. Elrod and Murphy[19] have reported a similar case operated upon in the same year. These authors believe that theirs was the first patient in this category to have been subjected to decortication.

R. B., a 14-year-old boy, developed sudden pain in the chest Feb. 25, 1947, while tobogganing. Dyspnea and shock followed rapidly. Upon admission to the hospital a short time later, signs of a massive left pleural effusion were present. Thoracentesis yielded pure blood and during the next three weeks repeated aspirations were done and 2,550 c.c. of blood were aspirated. During this period, blood transfusions totaling 2,000 c.c. were administered. When first seen by me, a small pneumothorax and signs of an organized hemothorax were present. The left lung and diaphragm were immobile.

Operation was performed April 1, 1947, in the manner previously described. At operation, the lung was immobile, and was collapsed approximately 50 per cent. After evacuating the pleural contents and dividing the pleural adhesions, it was possible to inflate the lung sufficiently almost to fill the pleural space. The peel was densely adherent over a 2 cm. area in the superior segment of the left lower lobe. This site was believed to be the source of the hemorrhage and the peel was not removed from this area. Elsewhere the peel separated readily, for the most part, by manual dissection. The parietal pleura was wiped with dry gauze, and the pulmonary fissures and diaphragmatic sinuses



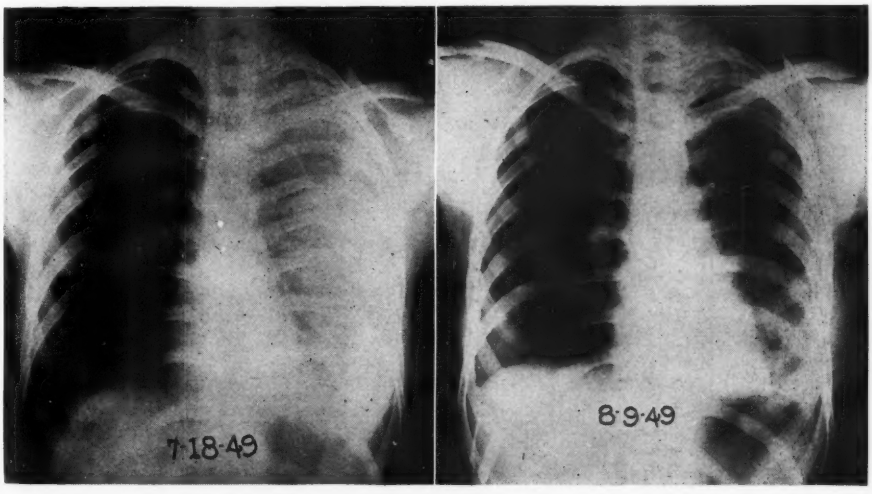
a. *b.* *c.*

Fig. 8 (Case 3).—The preoperative roentgenogram (*a*) and inspiration (*b*) and expiration (*c*) studies which were made two years and eight months after operation are illustrated.

were opened. The pleural space was drained with two catheters which were removed after forty-eight hours. Recovery was uneventful. Pre- and postoperative roentgenograms are illustrated in Fig. 8.

CASE 4.—The rapid re-expansion of the lung obtained in the following patient is of interest.

B. G., a 17-year-old white girl, had severe arterial hypertension, and underwent a two-stage thoracolumbar sympathectomy. During the second operation on the left side, an intercostal vein was opened, and the bleeding was arrested with Gelfoam. Severe intrapleural hemorrhage occurred postoperatively requiring numerous transfusions. Several aspirations were done by the surgeon but clotting occurred before the lung could be expanded. Decortication was done on July 28, 1949, five weeks after this operation. After preliminary pleurolysis, the peel was easily removed, using for the most part, blunt dissection. One small tear required a single cotton mattress suture. Drainage of the pleural space with two catheters was instituted, and the lung was fully expanded the following day. The patient made an uneventful recovery and was discharged from the hospital seven days after operation. Preoperative and postoperative roentgenograms of this patient are illustrated in Fig. 9.

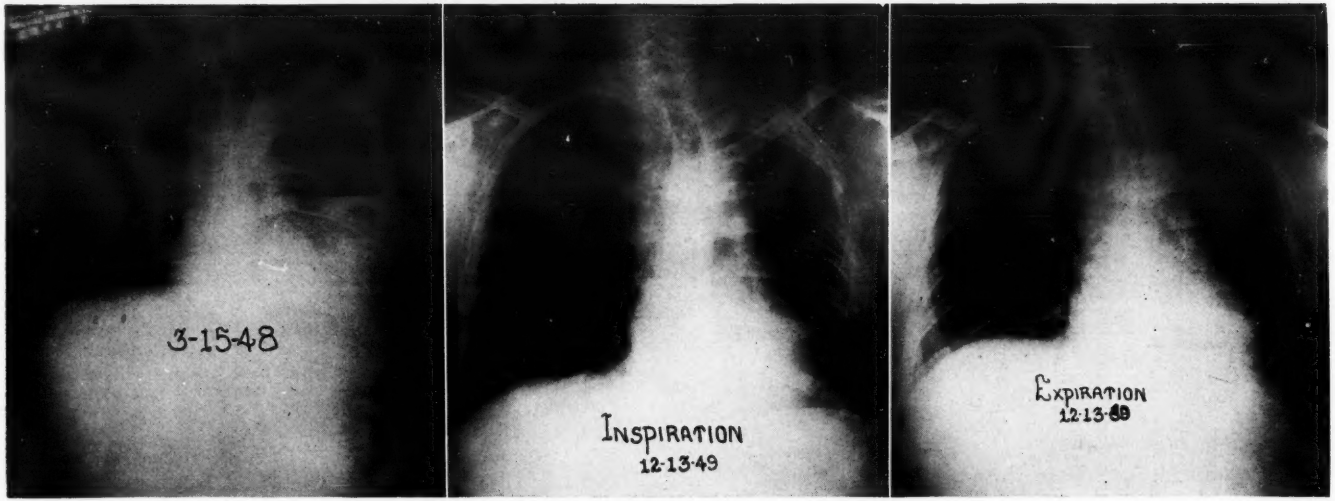


a. *b.*

Fig. 9 (Case 4).—Preoperative roentgenogram (*a*) and postoperative study (*b*) are illustrated. The latter film was exposed on the twelfth postoperative day.

CASE 5.—This patient's lung was collapsed for over eight years. Although the parietal peel was not removed, excellent mobilization of the ribs and left hemidiaphragm has followed operation.

J. S., a 25-year-old white man, had a left artificial pneumothorax induced on Jan. 24, 1940. Caseous pneumonic tuberculosis was controlled, and sputum was converted. Pleural adhesions were present and these were divided by a closed pneumonolysis on March 19, 1940. Pleural fluid was subsequently present on numerous occasions but he never developed empyema. All efforts to re-expand the lung were ineffectual. Decortication was done as previously described in Case 1 on April 16, 1948. A portion of the peel was left in place over the site of the disease in the upper lobe. The lung was fully expanded in forty-eight



a. *b.* *c.*

Fig. 10 (Case 5).—The preoperative roentgenogram (*a*) and inspiration (*b*) and expiration (*c*) studies made one year and nine months after operation are illustrated. Excellent mobilization of the ribs and diaphragm have followed operation. The parietal peel was not removed and the patient did not practice breathing exercises.

hours; convalescence was uneventful. The patient was transferred to another hospital six days after operation. At this writing he has been working for a period of eighteen months. Preoperative and postoperative roentgenograms are illustrated in Fig. 10.

CASE 6.—This patient had a pneumoperitoneum at the time of the operation. The procedure was well tolerated and prompt re-expansion of the lung occurred.

A. K., a 39-year-old married woman, developed pulmonary tuberculosis in April, 1944. A chest roentgenogram demonstrated an extensive bilateral exudative lesion with a cavity in the upper lobe of the left lung. Sputum was positive for acid-fast bacilli. An artificial pneumothorax was induced on the left side on May 14, 1944; adhesions were present and a closed pneumonolysis was done July 16, 1945. The patient's sputum was converted and she was discharged from the hospital Dec. 12, 1945. The patient was well until April, 1948; at this time she developed cough, fever, and weakness. Sputum was again positive and a roentgenogram demonstrated a cavity in the right lung. She was re-admitted to the hospital and streptomycin, 1 Gm. daily, was administered from April 8, 1948, until June 9, 1948. The infiltration in the right lung cleared, the cavity closed, and the patient was discharged from the hospital July 3, 1948. She remained well until July 26, 1949; at this time she developed fever and cough and a roentgenogram demonstrated a new cavity in the apical segment of the right lower lobe. Sputum was again positive. A pneumoperitoneum was induced July 28, 1949. The cavity closed promptly and sputum was converted within three months. During this period, attempts to re-expand the left lung were ineffectual. Decortication was performed Feb. 2, 1950. After division of the peel, the lung could be inflated sufficiently to fill almost completely the pleural space; it separated readily. Two small rents in the lung required closure with a 0000 cotton mattress suture. Drainage with two catheters was instituted as previously described. The lung was fully re-expanded the morning following operation. A small amount of drainage persisted and for this reason, the catheters were not removed until the second postoperative day. Convalescence was uneventful and the patient was transferred to another hospital six days after operation.

SUMMARY

In the foregoing, the factors that maintain pulmonary collapse in patients presenting indications for decortication are considered, and the importance of the role of pleural adhesions is emphasized. A change in the order of operative procedure is suggested, and a comparatively atraumatic and bloodless method of performing decortication is described. The procedure as outlined, is another application of an established surgical principle applicable to all dissections; namely, that adhesions which are least formidable should be divided initially, leaving those which are more difficult for the final step of the procedure.

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ADDENDUM

The operative technique described in this article has been used in decortication for tuberculous empyema; in this group it is believed that the parietal peel should be excised. A recent decortication for this disease was performed entirely without injury to the lung.

LOBAR AGENESIS OF THE LUNG

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AGENESIS of the lung is a rarely occurring congenital anomaly; however, lobar agenesis of one lung associated with an anatomic developmental abnormality of the bronchial tree is so exceptionally rare a manifestation that it is not specifically mentioned in the literature. During the past year the authors have had occasion to see two markedly similar proved cases of lobar agenesis of the lung and therefore present them as supplement to the data available on congenital lung malformation.

A search of the existing literature concerning cases which could represent a lobar agenesis of the lung yielded only two reports which might suggest such an anomaly if adequate proof had been available. Field[1] reported a case in which bronchography revealed a small left lung displaced posteriorly with a long main bronchus. There appeared to be no lingular branches. Confirmatory studies were not allowed by the parents of the patient. Ferguson and Neuhauser[2] reported a patient who was studied because of postulated atelectasis of the right middle and lower lobes. On bronchography a single bronchus was found on the right side which communicated only with the upper lobe. Although these two cases may have represented lobar agenesis of a lung, definitive anatomic proof is lacking.

A brief discussion of the embryology of the lung will serve to make more understandable the manner in which such an anomaly can occur. Two pulmonary anlagen may be differentiated: the epithelial and the mesenchymal. The earliest indication of the appearance of the epithelial anlage is the formation of a longitudinal groovelike evagination of the anterior wall of the foregut in the 3 mm. embryo. Fusion of the opposing edges of this evagination, termed the tracheoesophageal septum, begins at the caudal end and extends in a cranial direction, first splitting off the lung bud and then the trachea. When the embryo reaches the 4 to 5 mm. stage, the lung bud bifurcates; this represents the primordia of the main-stem bronchi. At the 7 mm. stage, the right-stem bronchus divides into three projections, and the left-stem bronchus divides into two projections. The bronchi grow by successive generations of monopodial branching into the thoracic cavities, pushing before them an investment of mesenchyma which adapts itself to the shape of the bronchial tree and fuses, ultimately, giving rise to the pulmonary lobes.[3]

A review of the literature pertinent to congenital pulmonary malformations reveals that a classification of agenesis of the lung was first made by Schneider[4] in 1912. Since that time the following definitions ordinarily have been employed as a basis for nomenclature:

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Agenesis of lung: where there is a complete absence of the lung and bronchi.

Aplasia of lung: where there is a rudimentary bronchus but no pulmonary alveolar tissue.

Hypoplasia of lung: where pulmonary tissue is underdeveloped in whole or in part of a lung.

In 1937, Hurwitz and Stephens[5] reviewed 34 cases of agenesis of the lung, and in 1944, DeWeese and Howard[6] increased this list to forty-four. Burger,[7] in 1947, reviewed an additional 10 cases which increased the list to fifty-four. Burger reported that 13 cases were to be found in the foreign literature, the details of these being as yet unobtainable. Since that time Field[1] has reported 3 cases, and Nesbit and associates[8] and Bowden[9] each have reported one. To date there are approximately 75 reported cases of agenesis of the lung.

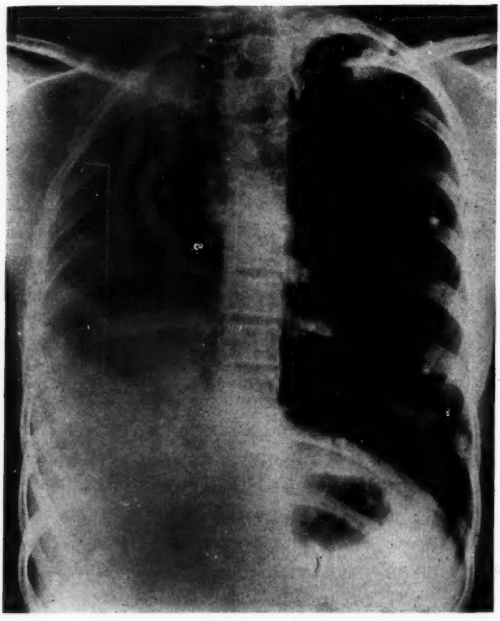

Fig. 1 (D. L. W.).—Roentgenogram showing deviation of the trachea to the right, elevation of the right diaphragm, dextrocardia, narrowing of the right intercostal spaces, and a diffuse density of the right hemithorax.

The majority of the cases reviewed in the preceding paragraph manifested severe degrees of agenesis, aplasia, or hypoplasia showing little or no functional lung tissue on the affected side. A variety of concomitant congenital anomalies were noted: cleft palate; agenesis of spleen, kidney and ureter; accessory thymus; esophageal atresia; tracheoesophageal fistula; diaphragmatic hernia; exencephaly; a variety of cardiovascular anomalies; hypoplasia of the face; dermoid of the eye; atresia ani, and incomplete lobulation of the remaining

lung. It is of interest to note that of these cases, 14 showed a unilobular or an incompletely fissured remaining lung. In one instance three bronchi were recorded as supplying such a unilobular lung. It is unfortunate that no mention is made of the number of bronchi in the other cases reported. This is not in agreement with the generally accepted concepts of the embryologic development of bronchi and lobes.

In the following two case reports, the diagnosis of lobar agenesis of the lung was established in the first instance by exploratory thoracotomy and in the second by autopsy.

CASE REPORTS

CASE 1.—D. L. W., an 11-year-old white girl, was admitted to Childrens Hospital on Aug. 8, 1949, with the chief complaint of a "bad right lung." This patient had a persistent cough associated with many colds since the onset of whooping cough at the age of 5 years. During the recent winter months she had many upper respiratory infections associated with high fever and shortness of breath.

On physical examination the thorax was asymmetrical, there being a respiratory lag of the right hemithorax. The point of maximal cardiac impulse was shifted to the right of the sternum. There was relative dullness of the right chest, associated with diminished breath sounds.

A roentgenogram of the chest (Fig. 1) revealed an elevation of the peripheral portion of the right diaphragm. There was a diffuse density throughout the right lung field, associated with a marked shift of the mediastinum, including the heart, to the right. There appeared to be a herniation of the left lung across the anterior mediastinum. On fluoroscopy limitation of diaphragmatic movement on the right was noted.

A bronchogram (Fig. 2, *A* and *B*) revealed but one bronchus communicating with a single lobe on the right side. A bifid bronchial stump was noted projecting anterior to the visualized lobe. This was believed to represent an occlusion of the middle and lower lobe bronchi with compensatory enlargement of the upper lobe associated with a fibrothorax. The possibility of lobar agenesis of the lung was suggested. Because of increasing symptoms an exploratory thoracotomy was performed on Aug. 11, 1949.

On exploration of the right thoracic cavity, the pleural space was found to be completely obliterated by dense fibrous tissue. The right lung consisted of a single lobe covered by a fibrous membrane, which was peeled from the visceral pleura without difficulty. There was a blind bifid outpouching of the main bronchus anteriorly about 3 cm. distal to the carina (Fig. 3). This was considered to be the undeveloped primordium of the right upper and middle lobe bronchi. The right pulmonary artery was found to be 5 cm. in length. There was no branching of this artery until it entered the lower lobe, when it divided into the usual segmental branches. The lobe was supplied by a single vein occupying the anatomic position of the inferior pulmonary vein. The superior pulmonary vein was absent. On completion of the operation, the right lower lobe completely filled the cavity. The patient's postoperative course was uneventful and she was discharged on the sixth postoperative day.

CASE 2.—D. V. S., a 2-month-old white male infant, was admitted to Childrens Hospital on Feb. 11, 1948, with the chief complaint of "right lung obstruction and vomiting." This patient had had persistent vomiting since birth. On a previous admission to another hospital barium studies had ruled out the possibility of pyloric stenosis. X-ray studies of the chest had revealed atelectasis of the entire right lung, dextrocardia, and compensatory emphysema of the left lung. There was no history of aspiration of foreign bodies. No cyanosis was seen at any time. There was no history of familial disease or of congenital abnormalities.

On physical examination there was a respiratory lag of the right chest. The point of maximal cardiac impulse was located near the right nipple line. A soft apical systolic murmur was present. Breath sounds were short and diminished over the right lung field, and absent over the area of cardiac dullness. The left chest was hyperresonant.

Fig. 2, *A* (D. L. W.).—Bronchogram revealing an anomalous right bronchial tree.

Fig. 2, *B* (D. L. W.).—Right lateral bronchogram which reveals undeveloped upper and middle lobe bronchi.

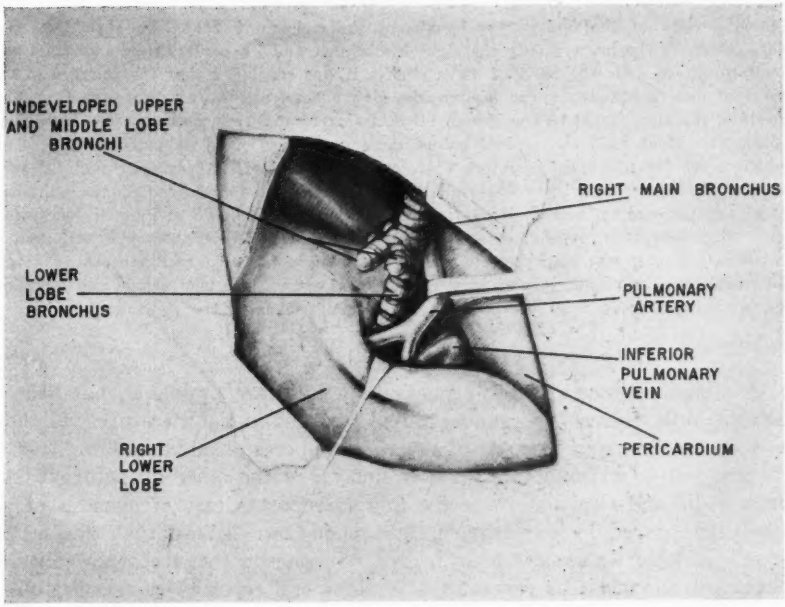

Fig. 3 (D. L. W.).—Illustration of the congenital anomalies and anatomic relationships as found during exploratory thoracotomy.

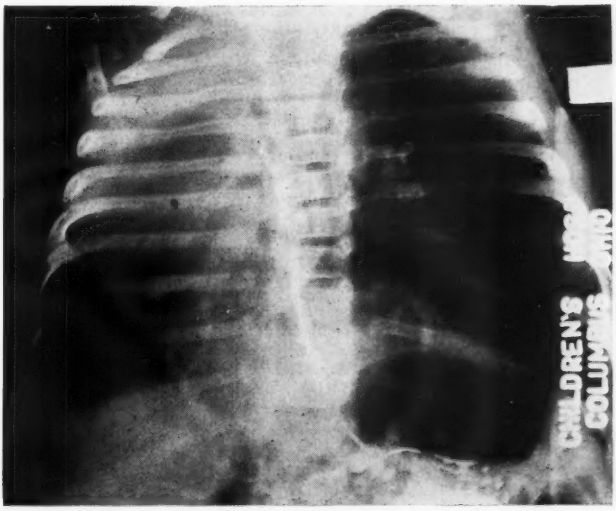

Fig. 4 (D. V. S.).—Roentgenogram showing right mediastinal shift, dextrocardia, and increased density of the right upper hemithorax.

Barium swallow and fluoroscopy showed the esophagus and trachea slightly deviated to the right. Chest roentgenograms revealed a mediastinal shift to the right (Fig. 4), with increased density of the upper three-fourths of the right lung field. The left lung was emphysematous. The heart was in the right hemithorax and its borders were indistinct and difficult to outline. On the basis of these studies it was concluded that the changes in the chest were due to massive atelectasis on the right; however, it was also suggested that agenesis of the lung should be considered. Bronchography and bronchoscopy were scheduled; however, the infant suddenly expired before these procedures could be performed.

Necropsy did not reveal the immediate cause of death. The pertinent findings were limited to the thoracic cavity. The right thoracic cavity showed diffuse fibrous adhesions between the pericardium and a single right lobe. The right middle and upper lobes were absent. The right-main bronchus communicated with the lower lobe without proximal branching. The left lung was emphysematous and herniated across the midline into the right hemithorax. The heart was located in the right chest. The final microscopic and anatomic diagnosis was lobar agenesis of the upper and middle lobes of the right lung.

DISCUSSION

Two similar cases of lobar agenesis of a lung are presented, parallels of which the authors have been unable to find recorded in the literature. In these two cases there was an agenesis of the right upper and middle lobes. One of these was proved by exploratory thoracotomy and the other by autopsy. Although Valle and Graham[10] were the first to report a case of agenesis of an entire lung proved by exploratory thoracotomy, we believe that this is the first case of lobar agenesis to be so proved. It appears that the abnormality of bronchial development as represented in these two reported cases must occur between the 5 mm. and 7 mm. stages of the human embryo.

SUMMARY

Two cases of lobar agenesis of the lung are reported, one of which was proved by exploratory thoracotomy, and the other by necropsy.

A discussion of the embryology and a review of the literature of lung agenesis have been presented.

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